Atomic Energy Control Board
P.O. Box 1046
Ottawa, Canada
K1P 5S9

Commission de contrôle de l'énergie atomique
C.P. 1046
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K1P 5S9

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COMPARISON OF THE RATIONALE USED IN SETTING OCCUPATIONAL EXPOSURE STANDARDS FOR IONIZING RADIATION AND HAZARDOUS CHEMICAL SUBSTANCES

by

D.M. Halton, Monserco Limited

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Research report

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ABSTRACT

The introduction to the study deals with the history and development of the regulations, recommendations, guidelines and standards as they apply to exposure, chemical and radioactive, in the workplace.

Ten chemicals which create significant occupational hazard are reviewed. They are toluene diisocyanate, hydrogen fluoride, n-hexane, carbon disulphide, cadmium, inorganic mercury, cobalt, nitroglycerol, silica and vinyl chloride. Each is discussed under the headings of physiological intake and elimination in humans, characteristics of acute and chronic toxicity, sites of occupational exposure and rationale for limits of such exposure.

Since radioactive substances yield ionizing radiation as the common hazard the treatment of the current permissible levels of exposure is somewhat simpler.

For hazardous chemical substances the American Conference of Governmental Industrial Hygienists (ACGIH) is the origin of recommended Threshold Limit Values (TLVs) which many jurisdictions have written into their regulatory framework. Standards for ionizing radiation sources, particles or vapour, arise from deliberations of committees of the International Commission on Radiological Protection. The growth of knowledge of injury due to ionizing radiation (X-rays) from the beginning of the century formed the basis of the recommended maximum occupational levels of airborne radionuclides.

Having set out industrial standards for exposure to hazardous substances and radionuclides, a detailed comparison is made. Exposure limits to ionizing radiation are sufficiently low to remove the appearance of directly related injury. It is expected however that low level exposure may have a stochastic effect, that is, there is the possibility of a slightly increased incidence of neoplasms in a large exposed population, but numbers will be too small to be able to attribute any particular case to the exposure. TLVs on the other hand, depending on the particular chemical, may be high enough in the workplace to permit some directly related signs or symptoms in the exposed individual.

A chapter on the scientific validity of the concepts used for establishing permissible limits is followed by the authors' conclusions, a detailed list of references, and a glossary of the rather specialized terms used in the field of occupational health and safety.

RÉSUMÉ

L'introduction porte sur l'histoire et l'établissement des règlements, recommandations, lignes directrices et normes sur l'exposition aux produits chimiques et aux matières radioactives au travail.

Dix produits chimiques qui représentent de graves dangers professionnels sont examinés : le diisocyanate de toluène, le fluorure d'hydrogène, l'n-hexane, le disulfure de carbone, le cadmium, le mercure inorganique, le cobalt, le nitroglycérol, la silice et le chlorure vinylique. Chacun de ces produits est examiné du point de vue de l'incorporation et de l'élimination physiologiques chez les humains, de leurs caractéristiques de toxicité chronique et aiguë, des lieux d'exposition professionnelle et de la justification des limites d'exposition respectives.

Comme les substances radioactives ont comme danger commun l'émission de rayonnements ionisants, le recours aux limites de doses admissibles actuelles est plus simple.

Pour les substances chimiques dangereuses, l'American Conference of Governmental Industrial Hygienists (ACGIH) a recommandé des valeurs limites de seuil (VLS), (appelées "Threshold Limit Values"), qui ont été incluses dans le cadre réglementaire de plusieurs autorités. Les normes pour les sources de rayonnement ionisant, sous forme de particules ou de vapeur, découlent des délibérations des comités de la Commission internationale de protection radiologique. Le progrès des connaissances sur les blessures causées par le rayonnement ionisant (les rayons X) depuis le début du siècle sert de fondement aux limites professionnelles maximales recommandées pour les radionucléides en suspension dans l'air.

Après avoir établi les normes industrielles pour l'exposition aux substances dangereuses et aux radionucléides, il est possible de faire une comparaison détaillée. Les limites de doses de rayonnement ionisant sont suffisamment faibles pour empêcher l'apparition de blessures directement reliées au rayonnement. Il est entendu toutefois que même faible, une dose de rayonnement peut produire un effet stochastique, c'est-à-dire qu'elle peut occasionner une faible augmentation de néoplasmes chez une grande population exposée, mais le nombre de cas ne sera pas suffisant pour permettre d'attribuer tout cas particulier à cette dose. Par contre, les VLS, selon le produit chimique particulier, peuvent être assez fortes en milieu de travail pour permettre de déceler quelques signes ou symptômes reliés directement à l'exposition d'une personne.

Le chapitre sur la validité scientifique des concepts utilisés pour établir des limites admissibles est suivi des conclusions des auteurs, d'une liste détaillée des références et d'un lexique des termes assez spécialisés du domaine de l'hygiène et de la sécurité au travail.

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EXECUTIVE SUMMARY

Purpose

In Canada occupational exposure standards are established to provide protection against workplace airborne chemical contaminants and ionizing radiation. Establishment of these standards requires review and interpretation of scientific data, development of concepts relating exposure and dose to biological harm, selection of workplace limits and practical application of the concepts and limits to the workplace situation.

The purpose of this report was to compare the rationales for establishing occupational exposure standards for ionizing radiation and hazardous chemical substances. Particular attention was given to the rationales used in establishing exposure limits. Ten chemicals known to produce adverse health effects after prolonged exposure were chosen for this study. The chemicals were toluene diisocyanate (TDI), hydrogen fluoride, n-hexane, carbon disulphide, cadmium, inorganic mercury, cobalt, nitroglycerol (NG), silica and vinyl chloride. The rationales used to establish the exposure limits for these ten chemicals were reviewed and then compared with the rationale used in setting limits for exposure to ionizing radiation.

Results

A. Workplace Chemical Exposure Standards

Most Canadian jurisdictions follow the limits and concepts developed by the American Conference of Governmental Industrial Hygienists (ACGIH). This is essentially the standard setting organization for the Western world.

i) Limits

Exposure Limits are set by reviewing the literature and determining an approximate dose-response relation for each chemical. The economic and logistic implications for industry are then considered. The exposure limit selected is a professional judgement which weighs the health consequences of overexposure against the costs to industry. The judgement

process embodies quite distinct criteria for assessing the acceptability of a health effect. There is little or no risk assessment or data extrapolation involved in the process of setting these limits.

Three of the chemicals reviewed in this report, namely carbon disulphide, nitroglycerol and silica have limits which in all likelihood would cause serious or fatal disease in some workers. Hydrogen fluoride has a limit which minimizes the occurrence of fluorosis. No definition of 'minimize' is given. TDI has limits which cause debilitating respiratory sensitization in some workers and threatens their employment security. One of the exposure levels for cobalt is set at a value known to produce disease in test animals. Only three of the ten chemicals reviewed, namely n-hexane, cadmium and mercury have any known safety factor. Vinyl chloride appears to have a safety factor which cannot be quantified.

ii) Concepts

The limits established by ACGIH are based on the concept of threshold. This means that up to a certain maximum exposure health effects would not be expected but above this maximum or threshold toxicity would be induced. ACGIH refers to its limits as threshold limit values (TLVs). However, most of these limits are interpreted as time-weighted averages (TWAs). This means that the threshold of toxicity can be exceeded for certain periods of time provided that it is balanced by exposure periods of equal magnitude below the threshold. This exposure averaging is integrated over an eight hour working day or forty hour working week.

There is no scientific basis for integrating exposures in this way and the concept runs contrary to most toxicological evidence which suggests that it is periods of peak exposure which cause biological harm rather than average exposures.

The time-weighted average concept is based on the principle that the product of the concentration of airborne contaminant with time produces a constant toxicological effect. This concept has never been scientifically validated and is unlikely to be true for most chemicals.

ACGIH believes that all chemicals including carcinogens have thresholds.

Biological damage is not considered to be accumulative. Biological repair is considered to play a part in maintaining homeostasis during chemical exposures which cause limited biological damage.

iii) Practical Application

Most exposure limits are applied in the workplace as time-weighted averages. A few which are considered to be particularly acutely toxic have ceiling values which must not be exceeded.

There is no concept comparable to the as low as reasonably achievable (ALARA) principle used in radiological protection.

The limits for workplace chemicals are established in terms of airborne concentrations or exposures. The idea of measuring doses within the body (known as biological exposure indices, BEIs) and the increased application of medical testing procedures for employees are recent and controversial developments. At the present time only six chemicals have recommended maximum concentration levels in exhaled breath, urine or blood serum.

B. Ionizing Radiation

i) Limits

Occupational exposure limits and concepts in ionizing radiation are recommended by the International Commission on Radiological Protection (ICRP). These limits and concepts have generally been adopted internationally.

Both primary and secondary (or derived) limits are developed by ICRP. Establishing primary limits involves viewing the available human and animal data regarding the dose-response relation.

For people exposed to ionizing radiation in the workplace there is a whole body annual dose limit of 50 millisieverts (mSv) (or 5 rems). This primary standard was originally established because of perceived genetic risks to mankind. In later years, experimental evidence indicated that the genetic risks were not as great as had been supposed. Instead, the appearance of late-occurring neoplasms was recognized as the principal risk from long-term exposure to low level ionizing radiations.

The hereditary (genetic) and carcinogen effects of ionizing radiation are referred to as stochastic. Other damage or ill health caused by ionizing radiation exposure is referred to as non-stochastic.

The primary standard for the annual dose limit is set well below the levels of radiation known to cause non-stochastic effects. In addition, the limit ensures that stochastic effects are kept within acceptable levels.

The primary limits are essentially judgemental values and appear to incorporate large but unquantifiable safety factors.

ii) Concepts

Non-stochastic effects are considered to have thresholds. Stochastic effects on the other hand are considered to occur without thresholds. The existence or non-existence of a threshold for hereditary or carcinogenic effects has never been demonstrated scientifically. However, the assumption that there is no threshold is a worst case scenario and gives precedence to human safety in a situation where there is scientific uncertainty.

Primary limits are established on the basis that, at low doses, biological damage accumulates with each radiation exposure. It is assumed that there is no biological repair. There is no scientific basis for this assumption, but once again, this is a worst case scenario and human safety is given precedence in an area of scientific uncertainty.

iii) Practical Application

Ionizing radiation uses the concept of dose as the basis for workplace limits even though only exposure is actually measured. However, the relation between exposure and dose in ionizing radiation appears relatively well defined from experimental investigations.

Secondary limits developed by mathematical modelling and data extrapolation are often based on very limited and tenuous knowledge about the metabolism of chemicals in man. However, these secondary limits are always developed in reference to the primary limits and any errors in modelling or extrapolation will not produce increases in morbidity or mortality.

A substantial number of people employed in work with ionizing radiation have annual exposures much lower than the 50 mSv annual limit. This is because workplaces are expected to apply the ALARA principle on the basis that any exposure involves some risk.

Non-stochastic effects would not be expected in a well-controlled work environment; also the risk of stochasic effects seems remote. In such circumstances medical testing of employees is unlikely to detect any diseases induced by ionizing radiation.

COMPARISON

	Chemical Standards	Ionizing Radiation Standards
Origin	ACGIH-Western World	ICRP-International
Protected Population	Those employed in manufacture or use of chemicals.	Individuals, their progeny and mankind.
Focus of Protection	Non-stochastic effects.	Stochastic effects.
Selection of Limits	Professional judgement balancing health effects with the costs to industry. Some limits set where health effects will occur in some people Often no safety factors.	Professional judgement essentially based on health considerations alone. Limits chosen on the inability to note effects plus worst case assumptions in areas of scientific uncertainty. Safety factors applied.
BASIC CONCEPTS		
Carcinogenic Effects	Have threshold.	Have no threshold.
Low Dose Effects	Are repaired.	Are not repaired, will accumulate.
Practical Application	Exposure measured (airborne concentrations)	Dose measured (but derived from measurement of exposure. Dose is not measured directly from body fluids or tissues).

COMPARISON cont'd

	Chemical Standards	Ionizing Radiation Standards
Practical Application	Implemented as TWA-based on CT=constant effect - no scientific basis.	Accumulated dose is tallied - and worst case assumptions used.
	NO ALARA	ALARA
	Moving towards medical monitoring of human body fluids and tissues.	Disease not expected.

Conclusions

The basis for setting limits for workplace chemicals and ionizing radiation exposures is essentially judgemental. The judgements made for ionizing radiation limits seem to have considerable advantages over many of those used for workplace chemicals. Ionizing radiation limits are chosen on the basis that there is no observable effect. Large margins of safety seem to be incorporated into the judgement process. Limits selected to protect against ionizing radiation exposure are based essentially on health considerations alone.

Workplace chemical exposure limits are often selected at levels where health effects are known to occur and it is expected that a certain, but undefined, proportion of the working population will suffer from these health effects. For in many limits there is little or no safety factor incorporated. Workplace chemical exposure limits attempt to balance the seriousness of the health effect with the costs incurred by industry in meeting a particular exposure limit.

From the evidence presented in this report it is apparent that the philosophy, concepts and limits developed and used to protect against ionizing radiation place a greater emphasis on preserving human health and well-being than do the comparable systems which establish limits for protection against hazardous chemicals in the workplace.

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1.0 INTRODUCTION

In May 1986, the Atomic Energy Control Board (AECB) requested a study which would look at the rationale used in setting occupational exposure standards for hazardous chemical substances. This rationale would then be compared with that used for setting occupational exposure standards for ionizing radiation.

The request was directly related to the AECBs responsibility for regulating the nuclear fuel cycle in Canada, including considerations of health and safety and other uses of radioisotopes and ionizing radiation emitters (e.g., particle accelerators).

The following report documents the study which was subsequently conducted by Monserco Limited under contract to the AECB.

2.0 SCOPE OF THE PRESENT STUDY

The present study describes the rationale used for setting occupational exposure standards in Canada for ten chemicals. The rationale for setting Canadian standards for ionizing radiation exposure is also examined. The processes and concepts of the two rationales are then compared and contrasted.

The study is based on a review of the existing literature on the health effects of the ten chemicals. Data was obtained using standard reference works on toxicology and a number of computerized data bases. The data bases consulted were Occupational Safety and Health (from Dialog), Registry of Toxic Effects of Chemical Substances (RTECS)(from U.S. National Library of Medicine), and the Hazardous Substances Data Bank (from U.S. National Library of Medicine).

Most Canadian jurisdictions (Table 1) have adopted the guidelines established by the American Conference of Governmental Industrial Hygienists (ACGIH). ACGIH often refer to the work of the U.S. National Institute of Occupational Safety and Health (NIOSH) in establishing its standards.

The documentation provided by three standard setting organizations was reviewed to seek the rationale for their recommended standard. ACGIH publishes its rationales in the "Documentation of the Threshold Limit Values". NIOSH publishes its rationales in a series of criteria documents. The Ontario Ministry of Labour does not publish rationales but reviews the literature through consultants reports.

Where information was available from the World Health Organization, this was also reviewed. The data from WHO have no pertinence to the standard setting system in Canada, and were included only for completeness.

Other reference sources were consulted where appropriate. Particularly useful was Schrecker's[Sc86] work on occupational exposure limits and Taylor's[Ta71] work on radiation protection standards.

The radiological section of the report traces the history and development of radiological protection standards using publications of the International Commission on Radiological Protection (ICRP) and other appropriate reference sources. Canadian authorities use the standards and concepts developed by ICRP as the basis for the ionizing radiation standards in Canada.

The report compares the rationales for setting exposure standards for chemicals and radiation. It also gives some insight into the scientific basis or validity on which these standards are established.

The final section of this reports presents the conclusions of the study.

3.0 HISTORY OF EXPOSURE LIMITS FOR WORKPLACE CHEMICALS

The concept of exposure limits for gases, or chemicals dispersed in air originated in Germany. In 1883 Gruber(Gr83) published results of exposing animals to various concentrations of carbon monoxide. He concluded that

> "...the limit of noxiousness for carbon monoxide is in all probability at a dilution of 0.05, but certainly at a dilution of 0.02%".

His figures correspond to airborne concentrations of 500 and 200 parts per million respectively. To confirm the results of his animal experimentation, Gruber himself inhaled 200 parts per million of carbon monoxide for three consecutive days. He reported no adverse reaction.

Lists of permissible exposure concentrations were subsequently published by Lehmann et al at Munichs' Hygienic Institute during the period 1886 to 1936. The data were produced from a series of short-term animal exposure studies. These investigations formed the basis for exposure standards for a number of chemicals used in industry at that time(Le11).

A further significant contributor was Kobert, who in 1912, published a list of 20 exposure limits(K012), again based on animal experimentation.

In North America interest in occupational exposure limits began in the early 1920's. In 1921 the U.S. Bureau of Mines published exposure limits for 33 compounds using much of the information from Kobert's work.

In the period of 1927 to 1947 there were at least 10 reports by German and American authors documenting permissible exposure limits for industrial chemicals(Sa27,Sa29,F131,Le38,Bo40, Ga43,Co45,Sc47,Vo37). A notable contribution was that of Cook (Co45) who carried out a literature review and published a list of exposure limits for 136 chemicals. Many of Cooks' recommendations were based on the earlier work of German scientists. Several exposure limits used in industry today can be traced back to the experimental data presented in early German publications.

Until the mid 1940s authors generally referred to their recommended exposure limits as maximum allowable concentrations (MACs). Most of the limits were based upon studies of acute toxic effects in animals. Frequently they recommended the

lowest concentration which produced a noticeable effect in animals(Sc86). Other limits used the smallest concentration which caused irritation in human subjects. A very few took into consideration the possible consequences of prolonged exposure even though long-term exposure to some chemicals such as lead, mercury, benzene and granite dust were all known to cause chronic diseases(He27,New21,Tu24,Gr26, Ru29).

As exposure limits developed, concern was expressed about using animal acute toxicity testing as the basis for determining workplace limits. Several people in the field pointed out that human workplace exposures occur day after day over many years and do not parallel acute toxicity testing conditions(He43).

Most tables published after 1935 showed a shift of emphasis. Figures were recommended with the implication that they would provide protection even after repeated exposures(Sc47). Since both animal experimentation and human data were mostly lacking, the basis for these figures was often little more than a rule of thumb. According to Cook(Co69).

> "...it was suggested as a rule of thumb that, where a given concentration was safe for eight hours, the acceptable concentrations for weeks or months might be taken as a fourth of the eight hour value."

In the late 1940s, professional organizations began to take an interest in workplace exposure limits. The American Standards Association, forerunner of the American National Standards Institute, (ANSI) issued a number of air standards. About the same time the National Conference of Governmental Industrial Hygienists, forerunner of the American Conference of Governmental Industrial Hygienists, (ACGIH) formed a committee on chemical agents to review pertinent data and propose exposure standards(Co50).

Over the next few years, standard setting for workplace chemical exposure limits was pursued by ACGIH and by ANSI. The ACGIH became the dominant organization in this process and eventually referred to its standards as Threshold Limit Values (TLVs). The air standards set by ANSI were referred to as Maximum Allowable Concentrations (MACs). For a number of years the terms TLV and MAC were assumed to mean the same and were used interchangebly.

The idea that exposure limits should be 'threshold limit values' is directly traceable to the famous observation by Paracelsus' (1493-1541):

> "What is there that is not poison? All things are poison and nothing is without poison. Solely the dose determines that a thing is not a poison".

Paracelsus was a physician who preferred to treat diseases by administering metals to his patients. He was severely criticized by the medical community who believed that only natural herbs had curative properties. They accused Paracelsus of using poisons. His published response to those criticisms produced the first recorded thoughts on the dose-response relationship(De86).

Put simply, this relationship states that the degree of adverse health effects depends on the dose received, and it also implies:

> "That a toxic substance can be reduced to such a low concentration that it has no effect on health(Ke82)."

This low concentration which has no effect on health is sometimes referred to as a no-effect level (NOEL). The favoured term in occupational hygiene is threshold level.

It is often considered that occupational exposure limits represent a 'safe' value below which no health problems will occur. Thus, determining the threshold limit is often considered as the founding principle for establishing a workplace exposure level. In reality, thresholds are difficult to determine with any precision. For chemicals causing cancer a threshold may not exist.

In 1953, ACGIH added a preamble to its list of TLVs, indicating without further explanation, that the values cited were intended as averages for an eight-hour working day. This fumdamentally changed the concept of TLVs. Previously they were considered to be the same as MACs namely, ceiling values below which all workplace levels must fluctuate. Now TLVs were not ceiling values. They were averages over an eight hour day, meaning that the 'threshold' limit could be <u>exceeded</u> for certain periods.

It is singularly odd that this dramatic shift in TLV interpretation was unexplained at the time of its introduction and still remains a mystery today. However, it can be surmised that the concept of TWA was probably advocated by one, Herbert Stokinger who was a very influential member of the TLV committee in 1951-1962. From 1962-1977 he was chairman of the committeee and his personal philosophies on exposure limits have had a profound impact on the standard setting system(St72,St70).

Given the historical origins of recommended workplace exposure limits, the ACGIH use of the term 'threshold limit value' is a little misleading. It implies that the levels it recommends are 'thresholds' below which no ill health effects will occur. In fact, many of the TLV's are based on the lowest level that effects do occur in animal or human experience. Further, the interpretation of TLVs as time-weighted averages, means that the health effect 'threshold' can be exceeded. The term 'threshold limit' seems to be a misnomer in this context.

Cook has summarized the history of occupational exposure limits for chemicals in the U.S.A. and has identified three development stages(Co69):

1. Standards based on short-term animal exposures;
2. standards to protect against long-term exposures; and
3. standards which relate the concentration to the duration of exposure through time weighted averages.

By 1968 ACGIH provided exposure limits for a total of 440 chemicals. It is of interest that out of these 440, 50 of the recommendations were identical to those published by Cook in 1945. Today virtually the entire standard setting system in the western world originates from the philosophy and recommendations of ACGIH. Individual jurisdictions may vary the specific figures for exposure, but in nearly all instances, the documentation supporting the choice of those figures is that of the of ACGIH. Of the many thousands of chemicals used in todays workplaces, only around 600 currently have TLVs assigned to them.

In Canada the provinces have jurisdiction in occupational health and safety except for certain classifications of federal employees or interprovincial transport operations. Ontario has begun to legislate workplace exposure levels. Other provinces have less legislation in this area or use a different approach to the control and enforcement of workplace exposures(Mo82). In setting guidelines or standards for workplace chemical

exposures all provinces seem to rely substantially on the recommendations of ACGIH(Lo82). Ontario, Alberta and British Columbia have produced their own standards for a few chemicals. How these few standards were developed in Alberta and British Columbia is not known. Ontario commission's consultants reports to collect background information for its standards.

4.0 PRESENT SYSTEMS FOR RECOMMENDING WORKPLACE CHEMICAL EXPOSURE LIMITS

4.1 Threshold Limit Values (TLVs)

Threshold limit values are recommended by the TLV committee of the ACGIH. This committee is a body of professionals with expertise in the areas of occupational hygiene, toxicology, medicine, and other sub-specialties of occupational health. There is no obvious critical review of their standard setting process from government or labour. However, industry is consulted and exerts influence. The process was summarized by Stokinger in 1969(St69):

> "Procedures used by the committee take three forms: (1) the chairman and members of the appropriate subcommittee hold a meeting with industry's physicians and industrial hygienists and review their experience. This procedure is used where the data has not been assembled or published. ... (2) Where the data or reports have been published, these are reviewed by the chairman and the committee and the action taken is that mutually agreed upon by industry and American Conference of Governmental Industrial Hygienists by letter correspondence. ... (3) Active cooperative projects with industry... are entered into whereby industry supplies the health records or clinical data for review, or active toxicologic research investigations are made ... in conjunction with clinical and environmental data obtained by industry."

Later he went on to say:

> "...industrial hygienists and toxicologists of some ... companies serve as consultants to the Committee ensuring first-hand information knowledge."

As Schrecker points out, this consultative procedure probably owes its origins to the period in which consultation with employers and the use of moral persuasion were virtually the only avenues open to industrial hygienists trying to keep exposure levels within safe limits(Sc86).

The term threshold limit value is copyrighted by ACGIH. No other organization can apply this terminology to its workplace exposure standards. In the introduction of the TLV booklet(TLV85), ACGIH states that:

> "Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.
>
> Threshold limit values are based on the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance; protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may form the basis for others."

The Threshold Limit Value - Time-Weighted Average (TLV-TWA) is defined as that concentration for a normal 8-hour workday and a 40-hour workweek to which nearly all workers may be repeatedly exposed day after day without effect. Nowhere does ACGIH specify what is meant by "nearly all workers".

In occupational hygiene, the 8-hour time-weighted average is calculated by multipling the airborne concentration of the contaminant by the duration of the exposure so that for any given chemical:

$$TWA = \frac{C_1 T_1 + C_2 T_2 \text{ ------- } C_n T_n}{8}$$

Where C_1 is the concentration in air and T_1 is the duration of the exposure in hours. C_2 is the concentration at a different point in the 8-hour shift for a period of T_2 hours.

Until recently, the scientific basis of TWA has never been questioned. Despite the absence of any adequate explanation for its introduction, the concept was rapidly accepted by the occupational hygiene community. In the past, the major concerns expressed about TWA related to its possible misuse or too literal interpretation rather than its scientific validity. For example, a literal interpretation of time-weighted average would allow for the exposure of a worker

to very high concentrations of a chemical for say 1 hour, provided the time-weighted average figure could be met by non-exposure to the chemical for the next 7 hours.

ACGIH has made several attempts to accomodate such ambiguities in the time-weighted average concept. These efforts have taken three forms.

1. Ceiling Values:

Starting in 1963, ACGIH began assigning certain TLVs with a "C" notation (for ceiling). The TLV-C is defined as the concentration that should not be exceeded during any part of the working exposure. All workplace levels should fluctuate below this ceiling. It is independent of TWA. In other words for some chemicals there has been a return to the concept of a 'MAC' exposure limit.

2. Threshold Limit Value - Short-term Exposure Limit (TLV-STEL):

A STEL is viewed as a concentration to which workers can be exposed for a short period of time without suffering from 1) irritation, 2) chronic or irreversible tissue damage or 3) narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency, and provided that the daily TLV-TWA is not exceeded. It is not a separate independent exposure limit, rather it supplements the time-weighted average limit where there are recognized acute effects from a substance whose toxic effects are primarily of a chronic nature.

STELs are recommended only where toxic effects have been reported from high short-term exposures in either humans or animals.

A STEL is defined as a 15-minute time-weighted average exposure which should not be exceeded during a workday even if the 8-hour time-weighted average is within the TLV. Exposures at the STEL should not be longer than 15 minutes and should not be repeated more than 4 times a day. There should be at least 60 minutes between successive exposures at the STEL. An averaging period other than 15-minutes may be recommended when this is warranted by observed biological effects.

Put simply, a STEL is a limited-time ceiling value or MAC, which must be incorporated as part of the TWA.

3. Excursion Limits:

These represent an attempt to specify the extent to which a time-weighted average concentration can be exceeded. At least 2 methods for calculating permissible excursions for those substances not covered by a STEL or a ceiling value have been suggested. The first of these is shown in the table below and linked the excursion factor to the 8-hour TWA:

TLV (8-hour TWA)	Excursion Factor
0 - 1 (ppm or mg/m^3)	3
1 - 10	2
10 - 100	1.5
100 - 1000	1.25

This table would be interpreted by saying that the maximum permissible concentration for a substance with a 8-hour TWA of 5 ppm would be 10 ppm (5 x 2) Similarly for a substance with an 8-hour TWA of 100 ppm the excursion limit would be 150 ppm (100 x 1.5).

It is interesting that with respect to excursion limits, ACGIH is prepared to admit;

> "...while no rigorous rationale was provided for these particular values, the basic concept was intuitive: In a well controlled process exposure, excursions should be held within some reasonable limits. Unfortunately, neither toxicology nor collective industrial hygiene experience provide a solid basis for quantifying what those limits should be."(TLV85)

ACGIH's table of excursion limits were criticized by Henschler(He81). He noted that excursion factors do not take into account well established rules of the dose response relationship. Henschler's criticism ignores the entirely arbritary nature of the excursion factors.

Apparently recognizing the shortcomings of this excursion factor approach ACGIH proposed to replace it with one based on a belief that;

> "...the maximum recommended excursion should be related to the value generally observed in the actual industrial processes."(TLV85)

Based on surveys of the general distribution of exposure values observed in industrial hygiene surveys conducted by the U.S. National Institute for Occupational Health and Safety (NIOSH), the new excursion limit recommendation was:

> "Short-term exposures should exceed 3 times the TLV-TWA for no more than the total of 30 minutes during a workday and under no circumstances should they exceed 5 times the TLV, provided that the TLV-TWA is not exceeded..."

Schrecker(Sc86) points out that the replacement of excursion factors with the new excursion limit recommendations derived from NIOSH data is no less arbritary. Further, it tends to rely on what is essentially an engineering judgement about how well controlled processes ought to operate rather than assessing workplace exposures on the basis of permissible exposure limits. The method for defining excursion limits clearly remains unsatisfactory.

4.2 Carcinogen Classification

Quite separate from the TLV standards ACGIH classifies some chemicals with the notation A1 which means they are confirmed human carcinogens. Some of these carcinogens have a TLV; others do not. On this point ACGIH states:

> "All steps must be properly taken to keep exposures to a minimum. Workers exposed to A1 carcinogens without a TLV should be properly equipped to insure virtually no contact with the carcinogen."

A second category of chemicals exists with the notation A2. This means they are suspected of having carcinogenic potential for man. The category is based on:

1. Limited epidemiological evidence, exclusive of clinical reports of single cases.
2. Demonstration of carcinogenesis in one or more animal species by appropriate methods.

The majority of those substances listed in the A2 category have TLVs. ACGIH specifies that for the A2 category:

> "Worker exposure by all routes should be carefully controlled to levels consistent with the animal and human experience data, (see ACGIH Documentation), including those substances with a listed TLV."

ACGIH has obviously had some problems rationalizing the use of TLVs for carcinogens and it explains:

> "In order to determine in which category to classify an experimental carcinogen for the purpose of assigning an industrial air limit (TLV), an approximate threshold of neoplastic response must be determined. Because of practical experimental difficulties, a precisely defined threshold cannot be attained. For the purpose of standard-setting, this is of little moment, as an appropriate risk, or safety, factor can be applied to the approximate threshold, the magnitude of which is dependent on the degree of potency of the carcinogenic response."

Implicit in this explanation is the belief that carcinogens do indeed have thresholds, and that such thresholds can be determined, at least approximately, in order to apply an appropriate safety factor. These seem to be somewhat generous assumptions.

In order to assign a TLV, carcinogen classification, or both to a chemical, ACGIH conducts a review of the literature. These literature reviews are published under the title "Documentation of the Threshold Limit Values".

4.3 Biological Exposure Indices (BEIs)

Reference to biological limit values has appeared in the preface of ACGIH's TLV list since 1973, in the 1985-86 TLV booklet, ACGIH has proposed to establish a few:

> "...biological exposure indices (BEIs) which represent warning levels of biological response to the chemical, or warning levels of the chemical or its metabolic products in tissues, fluids or exhaled air of exposed workers, regardless of whether the chemical was inhaled, ingested or absorbed via skin ... introduction of the BEI is a step in the evolution of the concept of TLVs. The BEI provides the health personnel with an additional tool to provide protection for the worker ... the BEI is

> considered supplementary to an airborne TLV ... TLVs are a measure of the composition of the external environment surrounding the worker. BEIs are a measure of the amount of chemical absorbed into the body. The concept of the BEI is particularly useful in evaluating exposures to substances with significant absorption through the skin."

To date, ACGIH has proposed BEI values for only ten chemicals where it it thought BEIs could be used as a guide to "safe exposures to toxic chemicals". The introduction of the first few BEIs has proved controversial and their future development is uncertain.

4.4 Maximum Allowable Concentrations (MACs)

Prior to the introduction of time-weighted averages, exposure limits in the United States were expressed as maximum allowable concentrations. Occupational hygienists interpreted MACs as ceiling values. They were seen as concentrations which represented a definitive threshold limit below which no effects would occur, above which toxicity could be expected.

Despite the absence of any sound rationale for shifting from MACs to TWAs, the TWA concept was accepted throughout the western world. However, there has been a marked reluctance to accept TWA in the Soviet Union and Eastern bloc countries where the use of MACs prevails. Sanockij in 1972 observed that Soviet MACs were:

> "...maximum concentrations that must not be exceeded during the shift."

He stated:

> "...those who support the need for averaging the concentrations usually argue that the biological effect is determined by the dose of the poison that enters the body. Fluctuations in the concentration of poisons of cumulative-type, according to these authors, are thus of no importance, since they are smoothed out within the organism. However, this contradicts the evidence that more severe lesions result from the intermittent actions of pathogenic environmental factors than from their continuous uniform action."(Sa72)

Levels for MACs used in the Soviet Union and Soviet bloc countries are generally lower than those levels quoted as TWAs in the ACGIH booklet. It is impossible to say whether such stringent exposure levels are actually enforced.

It is not clear from the Russian literature who selects the recommended MAC values, but it seems to be a body of professional experts in the area of occupational hygiene. It is presumed that government has substantial input into the process.

4.5 Designated Substances

Since the occupational health and safety act of 1978, the Ontario Ministry of Labour has produced a series of regulations specifying permissible exposure levels in the workplace. Codes for respiratory equipment, for determination of the workplace contaminant in body fluids, for the measurement of the airborne contaminant and for medical surveillance are all detailed in the regulations.

The permissible exposure level is stated as a time-weighted average. At the time of writing, nine substances had been designated and legislation was planned for others. Ontario has made more progress than other provinces in the area of exposure limit legislation, but not all provinces use legislative approaches (Table 1).

The Ontario Ministry of Labour does not publish any documentation which describes the basis for the selected exposure limit. Often the MOL will commission two consultants reports. One report will look at the health effects of the proposed designated substance. The other will survey plants using the chemical and may report on the feasibility of attaining a particular airborne standard within those industries.

The exposure limit figures selected are often the same or close to those recommended by ACGIH, even though the process for developing the standard is much more open and permits public debate. There are six distinct phases in the process.

> Phase 1 - involves the assembly of preliminary data and initial consultation with industry and labour.
>
> Phase 2 - involves publication of a "Notice of Possible Designation" in the Ontario Gazette and daily newspapers followed by an analysis of public comments.

Phase 3 - preparation and publication of a health effects document for comment.

Phase 4 - publication of a proposed regulation in the Ontario Gazette, followed by an analysis of public comments and possible revisions.

Phase 5 - a public meeting is held at Queens Park at which the proposed regulations are explained and comments are received.

Phase 6 - a final report on the final proposed regulation and codes is forwarded to the advisory council on occupational health and occupational safety for review. The Ministry of Labour then submits the regulations to the cabinet for approval. This process is represented in more detail in the flow chart, Figure 1.

Unlike the systems used by ACGIH the Ontario government attempts to achieve a standard through a process of concensus and discussion with the parties concerned. Business, government, labour and the general public can all have input.

4.6 NIOSH - Criteria for Recommended Standards

The National Insitute for Occupational Safety and Health is a U.S. Federal organization which essentially acts as the 'research arm' for the Occupational Health and Safety Administration (OSHA). OSHA is the Federal enforcement agency for matters relating to the workplace.

NIOSH does not legislate chemical exposure limit standards but makes recommendations to OSHA on what those standards should be. These recommendations are published in a series of criteria documents. These documents review the scientific literature on the health effects of exposure to a particular workplace chemical. NIOSH then recommends an appropriate airborne concentration based on its literature review and ostensibly, at least, on health considerations alone. The mandate of NIOSH is to protect all workers and political or economic factors are not supposed to enter the NIOSH review and recommendation process. OSHA may or may not follow the recommendations of NIOSH. Of 115 exposure limit recommendations made by NIOSH, only five have been adopted by OSHA. Most of the legislated exposure limits used by OSHA are taken from the 1968 ACGIH TLV booklet. A few have been updated. Generally speaking, NIOSH criteria documents review the same literature as the ACGIH "Documentation of Threshold Limit Values".

4.7 WHO - Environmental Health Criteria

The World Health Organization does not recommend workplace exposure standards for chemicals. By using international 'working groups' it has published forty or so Environmental Health Criteria documents which extensively review the literature on the selected chemicals. The basis for selection of the chemicals is unknown but they seem to represent those which have significant economic or environmental impact. The EHC documents are written to give member states access to essential evaluated information which offers a basis for national prevention or control action and for setting exposure limits consistent with health protection. The reviews published so far cover ground that is very similar to that covered in the documents by NIOSH and ACGIH.

Of the forty or so EHC documents planned for the future, over half relate to pesticides.

5.0 CHEMICALS CHOSEN IN THIS STUDY

Chemicals were chosen for the following reasons:

1. They are used in Canadian industry.
2. They have known significant health effects after long-term exposures.
3. Standards or guidelines are in existence.
4. As wide a variety of chemical families as possible were included.
5. As wide variety of chronic disease conditions as possible involving different organ systems were included.

Table 2 lists the chemicals selected and the chronic diseases which they cause.

In the subsequent sections that deal with the rationale for the exposure limits to these chemicals, emphasis is placed on documentation published by ACGIH. This is because many Canadian jurisdictions follow the ACGIH guidelines. Canadian data which shows notable departure from ACGIH is highlighted.

The ACGIH committee lists and briefly discusses the reports and publications which were used in establishing TLVs in its "Documentation of the Threshold Limit Values". They do not however, go into detail as to how the exact figures were chosen. The reader is left to surmise that certain publications and reports quoted assumed a precedence over others in the standard setting procedure, but exact details of which reports and why they were chosen are not specified. Further, it is evident in some standards that political and economic considerations had some influence. The scientific data in these cases does not rationalize the chosen exposure limit.

Where NIOSH or WHO documentation exist it is incorporated and compared with that from ACGIH and Canadian jurisdictions.

6.0 TOLUENE DIISOCYANATE (TDI)

6.1 Occupational Exposure

Exposure to TDI occurs in the manufacture of flexible polyurethane foams, rigid foams, polyurethane varnish coatings and in the production of certain types of adhesives and sealants.

The most commonly used form of TDI is a mixture of 80% of the 2,4-TDI and 20% of the 2,6-isomer.

6.2 Intake and Elimination

TDI mists and vapours enter the body through inhalation, skin or eye contact. Liquid TDI can enter through skin splashes, eye splashes or accidental ingestion.

There is little information on the metabolism of TDI in man or animals. Certainly a fair proportion of inhaled TDI is also exhaled. No information could be found on metabolites eliminated in the urine. Medical monitoring programs for TDI exposure do not use blood or urine samples in their clinical testing procedures. Only pulmonary functions tests are used.

6.3 Acute Toxicity

Inhaled TDI vapour or mist can cause irritation of all parts of the respiratory tract. Symptoms include a sensation of burning or irritation of the nose and throat, a choking sensation and a cough which may be recurrent and may produce sputum. There may be a soreness behind the breast bone and general chest pain(Ni73).

High levels of TDI vapour or mist may cause chemical bronchitis with severe asthma-like wheezing. The lungs may become inflammed and fluid may accumulate in them. In rare cases, this has proved fatal(Ni73). Symptoms may not appear until four to eight hours after exposure. Although discomfort may last for several weeks most people usually recover completely(Ka86).

The following effects have been reported in people exposed to TDI for 30 minutes[He62].

0.01-0.02 ppm	No odour or irritation was detectable.
0.05 ppm	The odour was detectable to the test subjects.
0.05-0.1 ppm	Slight irritation of the eyes, nose and throat. Eye and nose secretions in some subjects.
0.5 ppm	Eye and nose secretions in all subjects.
1.3 ppm (10 minutes only)	Heavy eye secretion, swollen eye lids, conjunctivitis.

A few hours after exposure subjects experienced inflammation of the respiratory tract mucous membranes with coughing and catarrh discharge.

Isocyanates react with skin and can cause marked inflammation[Ni73,Up80]. Prolonged skin contact causes redness, blistering and in some instances, burns. Skin tanning can occur[III80].

Splashes of TDI into the eyes cause irritation, swelling and watering of the eyes.

TDI vapours at greater than 0.05 ppm cause smarting and prickling sensations of the eye[He52].

6.4 Chronic Toxicity

Respiratory sensitization may develop in people working with TDI. Some become sensitized on their first exposure while others develop symptoms only after a period of days, months, or years[Ac84]. Once sensitized, TDI levels below 0.001 ppm can trigger a response[Be82]. This is far below current occupational exposure levels. Chronic sensitization to TDI may first appear as a cold or mild hay fever[Wo82]. Serious sensitization resembles bronchial asthma and presents symptoms of wheezing, difficult breathing, cough, shortness of breath

and chest tightness. These effects are caused by a narrowing of the airways of the lungs(Ni73,Ac84,We81). Occasionally these symptoms have been severe enough to require hospitalization(Ka79).

Several studies have shown that up to 25% of employees in some workplaces become sensitized to TDI(Ac84). There are conflicting reports about the recovery of sensitized people who are removed from any further TDI exposure. Some reports state that symptoms such as chronic bronchitis and wheezing continue for several years and are accompanied by a continued decline in lung function(Ni85,Ac84,Ad75). Other reports record complete recovery of lung function in sensitized people and no further symptoms with 70 days of complete removal from TDI exposure(Ni73).

The biochemical mechanisms which lead to chronic TDI sensitivity are not completely understood. It is known that an immune system response is involved(Be82). Both allergy prone (atopic) and non-allergy prone people become sensitized to TDI(Be82,Ge85,Ni85).

A progressive decrease in lung capacity may occur in people exposed for years to low TDI levels. This has been observed in employees exposed to average levels as low as 0.002 to 0.003 ppm. The effect is usually subclinical and goes unnoticed by most workers(Ac84,We77).

6.5 Rationale for Exposure Limit

For the purposes of standard setting for TDI the health effects to be considered are:

1. Respiratory sensitization - an acute or chronic effect.
2. Decreases in lung function - a chronic effect.

In most Canadian jurisdictions the TLV-TWA for toluene-2,4-diisocyanate is 0.005 ppm with a STEL of 0.02 ppm (Table 1). This is the level recommended by ACGIH. The recommendations of the Ontario Ministry of Labour in their regulation respecting isocyanates is slightly different(Mo80). They state that exposure to isocyanates be:

> "...reduced to the lowest practical level and in any case, shall not exceed 0.005 parts of the isocyanate per million parts of air by volume" (as a time-weighted average).

They then go on to state in the next section that:

> "Workers shall not be exposed to isocyanates which exceed 0.02 parts isocyanates per million parts of air by volume in any period of time."

The wording implies that in Ontario 0.02 parts per million is a ceiling level, rather than a STEL. This is an ambiguity . Essentially the guideline recommends two independent exposure limits - a TWA and a ceiling value. This has the potential to make interpretation, enforcement and compliance somewhat subjective.

Animal studies have not been useful in establishing a TLV for TDI since respiratory sensitization is difficult to produce. The ACGIH documentation extensively reviews the literature pertaining to TDI exposure. This literature consists mostly of studies of worker exposures. Unfortunately, the ACGIH documentation is not specific about which, if any, of these studies swayed the committee to choose a 0.005 ppm time-weighted average. They cite studies by Butcher et al(Bu77,Bu76) who reported that some people could react at 0.01 parts per million but not at 0.005 parts per million and this seems to have provided the basis for the TWA. However, this level is no protection for workers who have already become sensitized. Challenge tests with TDI of around 0.001 parts per million have produced asthmatic reactions in sensitized people(Ca69).

ACGIH recommends that the time-weighted average has a STEL limit of 0.02 ppm. This is based on the recommendations of NIOSH(Ni73), but neither the ACGIH Documentation nor the NIOSH criteria recommendations seem to have much science behind them, at least not from the viewpoint of preventing sensitization. Indeed, ACGIH states:

> "...no evidence exists that 0.02 ppm can be regarded as a no effect level for sensitization..."

and they cite the work of Peters et al(Pe68,Pe69) who suggest even a STEL of 0.01 ppm would be too high.

Not only does the 0.02 ppm STEL not protect against sensitization it almost certainly does not protect against decreases in lung function. A number of studies demonstrate that consistent exposure for several months to levels below 0.02 ppm caused marked decreases in lung capacity(Wi64,We74,We77,We82). In one study of 112 workers in a polyurethane plant only those in the lowest exposure group (less than 0.002 ppm) showed normal two year declines in lung function tests.

Given that ACGIH and NIOSH both cite reports demonstrating that a STEL of 0.02 ppm probably does not provide protection for those occupationally exposed, it is difficult to see the origin of the "rationale" for the recommended STEL figure.

The WHO is preparing a report on TDI, but at the time of writing, the report was only in draft form and could not be consulted for possible enlightenment on the STEL figure.

A clue to the origin of the figures comes not from ACGIH or NIOSH, but from a report submitted to the Ontario Ministry of Labour prior to the designation of isocyanates. In 1982, the MOL commissioned a study of TDI levels in a number of poly urethane manufacturing operations in Ontario(On82).

At that time, the TLV-TWA recommended by ACGIH was 0.02 parts per million. The authors of the MOL report were apparently instructed to comment on the feasibility of reducing the TWA to the level of 0.005 ppm. They reported that:

> "There were several plants in which the TDI or MDI (a related isocyanate) concentrations were above the 0.005 ppm. Indications are that a large percentage of plants will exceed the TLV if it were set at 0.005 ppm."

From their industrial hygiene walk through survey, they noted that:

> "Generally speaking...workers were not instructed in the proper handling procedures for isocyanates, improperly specified personal protective equipment was being used and there was a lack of knowledge of how to handle emergency spills."

Further, there appeared to be several cases of inadequate ventilation at process points. In other words, significant engineering changes would be required by industry in order to meet ventilation requirements for a 0.005 ppm TLV-TWA.

From the statements of the consultants report we can speculate that the polyurethane industry in Ontario was inadequately prepared either in worker training procedures, or in engineering controls to meet the requirements for a 0.005 ppm time-weighted average. This may explain why there is ambiguity in the Ontario designation for isocyanates and why there are essentially two independent limits specified. Consultation with the MOL on interpretation of the isocyanate regulation was helpful. The occupational health division stated that for

isocyanates an "As Low As Reasonbly Achievable" (ALARA) principle is applied in Ontario. New plants with modern technology would be expected to achieve the TWA, but older plants might not be able to do this(Pe86).

Although it is not stated in the NIOSH criteria or ACGIH documentation we can surmise that the TDI exposure levels chosen represent a compromise between the need to minimize the worker health effects and the ability of industry from an economic and logistical view point to meet with the recommended levels.

In a 1973 publication Stokinger and Scheel(St73) noted emphatically that:

> "...it is not possible at all times to control isocyanate exposure below permissible industrial air limits."

The case of TDI raises some difficult social issues. Sensitization may indeed be minimized or prevented by the 0.005 ppm TWA. The permitted STEL level (or ceiling level in Ontario) probably does not. Sensitization is not under normal circumstances a life threatening disease, but it does threaten employment security for affected workers. Once sensitized, all further contact with TDI must be prevented. Workers must be relocated in other areas of the plant. Often this cannot be achieved. Even relocation may be ineffective since low levels of TDI existing in other parts of the plant can trigger the asthmatic attack in a sensitized worker. Leaving the place of employment may be the only option.

7.0 HYDROGEN FLUORIDE

7.1 Occupational Exposure

Exposure to hydrogen fluoride gas occurs in the production of aluminum fluoride, triolite, uranium hexafluoride, elemental fluorine, aqueous hydrofluoric acid, inorganic fluoride salts, fluorocarbons and in alkylation processes. The fluxes used in some welding operations can generate hydrogen fluoride(Cc85).

Exposure to hydrogen fluoride liquid occurs in the production of fluorine compounds, cleaning iron and steel castings, etching and frosting of glass, the froth flotation of ores and washing sand free of iron. Small amounts of hydrogen fluoride are added to some commercial cleaning agents, and minor exposures may occur during their use.

7.2 Intake and Elimination

Significant amounts of hydrogen fluoride can be taken into the body by inhaling the vapour or by absorbing the liquid through the skin.

In most industrial usage exposure occurs largely through inhalation. The gas has a marked affinity for water and combines with mist or water vapour in the air as well as the moisture in the respiratory tract and eyes. At concentrations above 122 ppm hydrogen fluoride can combine with moisture on the human skin to produce a smarting sensation(Ma34).

Use of the dilute liquid may result in skin contact. Hydrofluoric acid rapidly and insidiously penetrates the skin at concentrations above 6%(Kl55). Absorption in this manner can cause severe poisoning. Skin contact with concentrated solutions has caused death(Di62,Yo75,Sc78,Bu73,Ni76,Br84).

In the body, hydrogen fluoride changes to fluoride ions, a significant amount of which is rapidly excreted in the urine. Of a given oral dose, approximately 20% appears in the urine within the first four hours and 50% is eliminated within a few days. Much of the remainder combines with bone and is only slowly removed from this tissue.

7.3 Acute Toxicity

The major effect of hydrogen fluoride on humans is due to its severe irritant and corrosive properties. Inflammation develops on any body surface which contacts hydrogen fluoride. The following toxic effects have been reported in humans exposed to hydrogen fluoride for brief periods(Ma63,Ma34,Ni76).

Up to 5 ppm	Skin reddening, sour taste in the mouth, slight irritation of the nose and eyes, nose bleeds.
61 ppm	Marked irritation of the lining of the nose and the eyes.
122 ppm	Tolerated for only one minute because of stinging of the eyes and smarting of the skin.
10,000 ppm and above	Choking, coughing, fever, shortness of breath and fluid accumulation in the lung, death.

In addition to effects on skin, nose and eyes as listed above, hydrogen fluoride can produce severe inflammation of the membranes inside the respiratory airways and the lung. Death caused by inhalation of high concentrations of hydrogen fluoride is probably due to severe acidic burning of the lung tissue which results in fluid accumulation in the lungs. This is quite distinct from fluoride poisoning which is the probable cause of death in cases of skin splashing(Ha84).

Hydrogen fluoride liquid can cause deep skin burns. It passes easily through pin holes in rubber gloves and may cause delayed agonizing burns of tissue beneath the nails. Burns from strong hydrogen fluoride (50%-70%) are felt immediately and can cause severe destruction of the tissue. Burns from solutions of 1% to 20% may not be felt for several hours(Ma63,Wh84).

The excruicating pain caused by hydrogen fluoride burns has been attributed to removal of calcium and magnesium from tissues and deposition of insoluble calcium fluoride. This leads to a relative excess of potassium in the tissues which causes nerve stimulation.

Death from fluoride poisoning may be related to a dramatic reduction in the amount of calcium available for use by the body(Mac85).

7.4 Chronic Toxicity

Hydrogen fluoride enters the body as fluoride. Fluoride is a bone seeker and excessive amounts will produce weakening and degeneration of the bone structure. Long-term fluoride poisoning may also cause heart, nerve and intestinal problems. The disease is called "fluorosis". Animal studies show that about half of a fluoride dose is deposited in the skeleton. In cases of continued long-term exposure an equilibrium or steady state is reached betwen blood fluoride levels and bone fluoride concentrations(Ne57).

Fluoride is not deposited permamently in the skeleton. It is mobilized slowly so that up to one-half may be removed and excreted over a period of two years. Under certain circumstances skeletal fluorosis may be slowly and partially reversible(Gr83).

7.5 Rationale for Exposure Limit

For the purposes of standard setting for hydrogen fluoride the health effects to be considered are:

1. Intense irritation - an acute effect.
2. Fluorosis - a chronic effect.

In most Canadian jurisdictions the workplace exposure limit for hydrogen fluoride is the TLV recommended by ACGIH. The present value is a ceiling limit of 3 ppm or 2.5 mg/m^3 as fluoride. All exposures must fluctuate below this level.

In their documentation for TLVs, the ACGIH committee cites the work of several authors. They note that Ronzani(Ro09) found no injurous action of fluoride in animals exposed for 30 days at 3 ppm. Stokinger *et al* found that animals tolerated 7 ppm of hydrogen fluoride with only mild irritation after repeated daily exposures(St49). However, at 17 ppm Largent noted damage to the lungs, liver and kidneys of animals repeatedly exposed(La61). He also reported experimental human exposures for 6 hours a day for between 10 and 50 days at concentrations as high as 4.7 ppm without severe effects. Redness of skin, burning and irritation of the nose and eyes were noted above 3 ppm.

In its criteria document for hydrogen fluoride NIOSH recommends a workplace environmental limit of 3 ppm (2.5 mg/m^3) as a time weighted average rather than a ceiling limit(Ni76). There are two further studies(Le67,Ry61) which report no pulmonary function changes or respiratory complaints below 3 ppm (2.5 mg/m^3). There is no obvious reason why NIOSH recommends a TWA while ACGIH recommends a ceiling. ACGIH presumably reasoned that the ceiling value was required for a compound with such pronounced acute toxicity.

The ACGIH committee observed that prolonged inhalation of hydrogen fluoride would probably lead to fluorosis, but they do not cite instances where this actually happened even though they appear in the literature(Wh80,Wa78). However, they cite a study by Derryberry et al(De63) which they interprete as indicating a threshold for small increases in bone density (an early sign of fluorosis) of below 4.3 ppm of hydrogen fluoride (3.38 mg/m^3).

The documentation concludes, "...the committee considers hydrogen fluoride a primary irritant, therefore a ceiling limit of 3 ppm is recommended. This should also minimize the occurrence of fluorosis."

From the available documentation it seems that the exposure standard for hydrogen fluoride is based on original animal experimentation carried out in Germany in 1909(Ro09) and since substantiated by further animal studies and human experience in the 1960's and 70's(Ry61,Le67,Ni76). It is quite evident that this exposure limit recommendation is intended only to prevent the irritation effects of hydrogen fluoride. Further, there is no indication of any safety factors in the standard that would allow for individual susceptibility or possible margins of experimental error.

It is quite clear from the concluding statement of the committee that the exposure standard is not intended to prevent fluorosis, only to minimize its occurrence. There is no indication in the ACGIH documentation of what is meant by 'minimize'. There is no definition of what "minimal" might mean in terms of an affected proportion of the worker population. There is no "As Low As Reasonably Achievable" (ALARA) principle either specified or implied in the ACGIH recommendation.

According to WHO(WHO84), severe fluorosis of the type causing degenerative bone disease is rarely encountered in industries today. There seems to be a consensus in the scientific community that 3 ppm will only produce minimal increases in bone density over a life time exposure(Mac85). These increases are only detectable by x-ray and in most cases have no clinical consequences. None of these details are raised in the ACGIH documentation and their emphasis is clearly on preventing the short-term irritation effects.

8.0 n-HEXANE

8.1 Occupational Exposure

Exposure to n-Hexane occurs during its use as a thinner and a solvent in the rubber, shoe, cosmetic and pharmaceutical industries. n-Hexane is also used during the manufacture of polyethylene, polypropylene, textiles, furniture and leather goods. In most of these uses n-Hexane is present as a mixture with other hexane isomers and a variety of solvents(Ma81).

n-Hexane is also a common component of gasoline, petroleum benzine and naphthas(Ma81,Ni77).

8.2 Intake and Elimination

The major route of occupational exposure is through inhalation of vapours. Absorption may also occur by contact of the liquid or vapour with the skin(Jo81,Ri78).

The majority of absorbed n-Hexane is eliminated unchanged from the body in exhaled air during the first few hours after exposure. The remaining n-Hexane is broken down into a variety of products and is excreted in the urine or exhaled as carbon dioxide.

n-Hexane has an affinity for fatty tissues and is temporarily deposited in fat storage areas of the body(Bo73). In rat studies, n-hexane is completely cleared from the body within four to eight hours(Bus77).

8.3 Acute Toxicity

Moderate overexposure can cause irritation of the eyes, nose and throat.

n-Hexane is an organic solvent and the short-term effects of exposure are typical of chemicals which act primarily as depressants of the central nervous system. The symptoms include dizziness, headaches, nausea and drowsiness. In cases of severe exposure unconsciousness and death can occur.

The following effects have been reported in humans exposed for brief periods to n-hexane vapours[Ne43,Pa29,Br77].

500 ppm	No observed effects in people without previous exposure.
880 ppm	Eye and throat irritation.
1400-1500 ppm	Slight nausea and headaches and irritation of the eyes and throat.
5000 ppm	Confusion, dizziness and drowsiness.

In industry symptoms such as dizziness and drowsiness have been observed when concentrations exceeded 1000 ppm.

No serious acute poisonings have been reported in humans exposed to n-hexane. The irritating nature of the vapour has provided sufficient warning of exposure so that major problems have been avoided.

8.4 Chronic Toxicity

Long-term overexposure to n-hexane has led to peripheral neuritis and peripheral neuropathy. Peripheral neuritis presents with symptoms of painful tingling or numbing in the fingers and toes. Usually this is associated with early nerve damage in the hands and feet[Ya67,Ja69,Ta75]. The condition may be accompanied by muscle weakness, tiredness, difficulty in pinching or grasping objects or stepping over curbs, loss of appetite, cramps and spasms in the legs, headaches, weight loss, muscle wasting and blurred vision. These symptoms develop very gradually over an extended period of time. If overexposure continues over a number of months or years, the nerve system in the hands and feet may die back completely. This advanced condition is known as peripheral neuropathy[He71]. Continued high level, long-term exposure can cause paralysis of the muscles of the legs and arms.

Outbreaks of n-hexane induced neuritis and neuropathy have been reported in workers in the production of shoes and cabinets and in fabric cleaning(Ab76). Incidents have been reported from Japan, Europe and throughout North America. Several cases of long-term solvent abuse involving n-hexane containing glues have been reported. In all instances signs and symptoms were indicative of peripheral nerve damage and paralleled occupational poisonings(Sh74).

In many cases the disease continues to worsen for some weeks after exposure stops. Mild to moderate cases generally show complete recovery within the year. Severe cases may also improve but sometimes tiredness and muscle weakness may persist for as long as three years after recovery. Full recovery may never occur(Sh74,Sp80).

8.5 Rationale for Exposure Limit

For the purposes of standard setting for n-hexane the effects to be considered are :

1. Sensory irritation (an acute effect).
2. Central nervous system depression (an acute effect).
3. Peripheral nerve damage (a chronic effect).

Since peripheral nerve damage occurs at levels below those causing sensory irritation or CNS depression, this chronic health effect has been the focus for standard setting.

In most Canadian jurisdictions n-hexane has a TLV-TWA of 50 ppm (Table 1). This is the level recommended by ACGIH. The ACGIH documentation for TLVs reviews many cases of occupational n-hexane exposure which have resulted in neurotoxicity.

They cite the report by Takeuchi et al in which four people exposed to petroleum benzine had symptoms of neuropathy(Ta75). The solvent used in this particular instance contained 12.5% of n-hexane and the authors estimate that the n-hexane vapour in the work room air did not exceed 210 ppm. All other reports reviewed by ACGIH and NIOSH involved levels of n-hexane that were at least double this value. There is no WHO report for n-hexane.

The documentation also quotes animal studies in which mice were exposed at 250 ppm of hexane for a year. Exposures were for 24 hours a day, 6 days a week and the hexane contained 65 to 70% of the normal isomer(In69,Mi67). In a further study by

Spencer[Sp79] rats were exposed 21 hours a day, 7 days a week for up to 8 months at 129 ppm of n-hexane and suffered no apparent nerve system dysfunction.

The ACGIH committee believes that in most instances solvents which led to n-hexane induced neuropathies were composed of between 50 and 70% n-hexane. They suggest a TLV-TWA of 50 ppm. This is half the value recommended by NIOSH[Ni77]. The NIOSH criteria document reviews almost identical reports to those quoted by ACGIH. There is no obvious reason why the NIOSH value is double that of ACGIH, but it would seem that the ACGIH committee has opted for a four-fold safety factor in their exposure limit recommendations. Although there are no details given as to why such conservatism prevailed in this instance, the level may reflect concern about possible synergism with other solvents. Such synergism has been demonstrated with several common solvents often used in association with n-hexane.

The TLV is apparently set to prevent chronic nerve damage and is based on the work of Takeuchi[Ta75] with an added four-fold safety factor.

n-Hexane is the only chemical in the series of ten discussed in this report for which a BEI has been proposed. The metabolism of n-hexane is relatively well studied. It is known to be broken down in the body to 2,5-hexanedione which is excreted in the urine. 2,5-Hexanedione is the metabolite believed to be responsible for peripheral neuropathy[Jo81,Pe81A,Pe80].

ACGIH bases its justification for a urinary BEI of 2,5-hexanedione by referring to the field studies of Perbellini et al[Pe81B,Pe81C] and Iwetall[Iw83]. These authors demonstrated a linear correlation between exposure concentration of n-hexane and a concentration of 2,5-hexanedione in urines collected at the end of a shift.

The BEI also recommends a maximum level of 40 ppm n-hexane in end exhaled air during the shift. This is based on a report by Brugnone et al[Br80] who noted a close correlation between exposure concentration and n-hexane concentration in alveolar air.

It is interesting that the BEI recommendations are at pains to establish that a relation exists between the amount of 2,5-hexanedione in urine (or the amount of n-hexane in exhaled air) to the workplace exposure as expressed as a TLV. There is no attempt in the BEI documentation to associate the urine or exhaled air levels with a dose-response relationship for neurotoxicity.

9.0 CARBON DISULFIDE

9.1 Occupational Exposure

The major use of carbon disulfide in today's industry is in the manufacture of viscose-rayon fibres. To a lesser extent it is used as a solvent for plastics, sulfur, rubber, phosphorous as well as various oils, resins and waxes. Carbon disulfide is also a component of some insecticides.

Exposure levels are set largely with reference to the viscose-rayon industry.

9.2 Intake and Elimination

The principal route of absorption in man is by inhalation of vapours. In addition, appreciable amounts can be absorbed through the skin. It is estimated that between 5 and 30% of absorbed carbon disulfide is rapidly excreted unchanged in the breath and perhaps less than 1% in the urine, the remainder is rapidly metabolized by the liver. The metabolic process is complex and ill defined, although some organosulfur derivatives have been detected in the urine. Little information is available on the identity of the metabolites and there is no indication that they have any quantitative relation to the amount of carbon disulfide absorbed.

9.3 Acute Toxicity

Several reports from the late 19th century document acute poisoning by inhalation of carbon disulfide in the workplace(Br1884,Ro1886,O102).

Toxic effects after exposure to greater than 500 ppm were characterized by a wide range of psychiatric disturbances ranging from excitability, confusion, extreme irritability, nightmares and depression, uncontrolled anger, manic delerium, hallucinations, and suicide or insanity. Concentrations around 5000 ppm rapidly produce central nervous system depression, respiratory paralysis and death.

The following effects have been reported in humans exposed for brief periods to carbon disulfide(WHO79).

960 ppm	Psychiatric symptoms, anger, paranoia, delerium, hallucination.
3200 ppm	Coma, death.

9.4 Chronic Toxicity

Prolonged exposure to carbon disulfide concentrations of 30 ppm and above has produced neurotoxic effects involving both the central and peripheral nervous systems. Peripheral neurotoxicity first appears as numbness and weakness in the legs and later, in the hands. This effect is slowly reversible after removal from exposure.

Prolonged exposure to greater than 50 ppm causes marked damage to both peripheral and cerebral arteries(Go40). No such effects have been reported in workers exposed to below 20 ppm.

Epidemiological studies in England and Finland(Ti68,To79) have established a relation between occupational exposure to carbon disulfide and an increased mortality from coronary heart disease. Workers exposed in viscose-rayon industries to levels frequently in excess of 20 ppm showed greater than two-fold increases in incidence of deaths attributed to ateriosclerosis. In the Finish plants workers had been exposed to 10 to 30 ppm during the 1960's and from between 20 and 60 ppm in earlier years.

A number of studies have indicated that carbon disulfide exposure may affect the microcirculation of the eye producing dot hemmorhages and microanurisms in the retina(WHO79).

9.5 Rationale for Exposure Limit

For the purposes of standard setting for carbon disulfide the health effects to be considered are:

1. Psychiatric disturbances (an acute effect).
2. Nervous system effects (acute and chronic effects).
3. Cardiovascular effects (chronic effect).

Since psychiatric disturbances occur at levels greater than neurological or cardiovascular effects, the latter have been the focus for standard setting.

In most Canadian jurisdictions the TLV-TWA for carbon disulfide is 10 ppm (30 mg/m^3) (Table 1). This is the level recommended by ACGIH.

The basis for the recommended exposure limit seems to originate from worker experience in the viscose-rayon industry. In particular, studies which showed significant excess mortality from cardiovascular disease due to prolonged exposure at 10 to 30 ppm(He73,To79,Ti68). Studies showing evidence of neurotoxicity(Se74) have also carried substantial weight.

Animal studies have not contributed to the standard setting process. Where such studies exist they are largely concerned with elucidating the mechanism of toxicity rather than establishing any dose-response relation.

Both the ACGIH committee and NIOSH(Ni77) base their recommended exposure limits upon the same documentation. However, NIOSH observed that since cardiovascular and neurologic studies indicate that 10 ppm is the lowest concentration causing demonstrated health effects, then a ten-fold safety factor should be included in the exposure limit recommendation. NIOSH recommend a 1 ppm TWA.

The WHO agrees that a safety factor is desirable(WHO79). They state that a 10 ppm TWA is the lowest level at which cardiovascular, neurological and neurophysiological effects can be found and that most toxic effects could be prevented by keeping the TWA below 10 ppm.

They go on to cite studies in the U.S.S.R. where workers exposed to 3 ppm for 10-15 years have shown no neurological or cardiovascular disorders.

The ACGIH committee was apparently unmoved by the NIOSH and WHO reports and did not agree that a ten-fold safety limit was necessary since they state in their documentation:

> "...the sense of the committee is that a limit of 10 ppm would be appropriate."

Once again, it is only possible to surmise the rationale behind the ACGIH recommendation. The data demonstrating cardiovascular and neurological effects at levels of 10 ppm and above is substantial. The absence of any safety factor in the ACGIH recommendation would suggest that considerations other

than health effects played a role in the development of their recommended standard. In this case, there are no clues as to whether these other factors involved the economic cost to industry or political considerations.

10.0 CADMIUIM

10.1 Occupational Exposure

Cadmium is a relatively rare metal occurring in the earth's crust in a proportion of about 0.55 grams per metric tonne. Geologically, it occurs mainly as green ockite (CDS) in association with zinc ore deposits such as sphalerite. It also occurs in association with other non-ferrous metal ores. Exposure occurs during mining and refining operations.

Cadmium has high corrosion resistence and is used in the production of alloys with copper, gold, silver, bismuth, nickel and aluminum. These alloys are used as protective coatings for other materials. Cadmium alone is used for corrosion resistant coatings of iron, steel and copper. Lesser amounts of cadmium are used in semi-conductors, photocells, in jewelery, in engraving processes and in the automobile and aircraft industries. Some cadmium compounds are found in fungicides, neomatocides and insecticides.

Cadmium has a relatively low boiling point when compared with other metals. This means that heating processes such as ore roasting or recycling of non-ferrous metals can cause cadmium to volatilize into the atmosphere. Releases of cadmium fumes from electroplating operations have also been reported(Be66).

Ontario's sole producer of pure cadmium is Kidd Creek Mines, which during the years 1980 to 1982 produced approximately 1.8 million kilograms.

10.2 Intake and Elimination

Inhalation is the major route of cadmium exposure in the workplace.

Inside the body cadmium is transported from the liver and lungs to the kidney where it accumulates and causes damage(Ti63). Cadmium deposited in the liver and kidney constitutes 50 to 60% of the total body burden. In occupationally exposed people appreciable amounts of cadmium are also found in the lung. The half-life of cadmium is estimated to be greater than 10 years and repeated daily exposure increases the cadmium accumulation in tissues(Fr74,Fr79)

10.3 Acute Toxicity

Inhalation of cadmium oxide fumes can result in chemical pneumonitis. Exposure to only 2 to 3 mg/m^3 produces this effect. There is little or no discomfort or irritation at the immediate time of exposure and lethal quantities can be inhaled without warning(Pa76).

It may take up to 10 hours following an acute exposure for effects to be noticed. Symptoms include shortness of breath, cough and tightness in the chest. Victims complain of substernal pain and a burning sensation in the chest. A flu-like condition may develop accompanied with fever and muscular pain in the back and the limbs. If exposure has been severe pulmonary edema may develop within 24 hours.

Victims of small exposures may recover within a few days but in some instances the shortness of breath may be progressive. At least one case of acute cadmium fume poisoning has produced renal necrosis(Be66). There is very little data on dose-response relations for acute exposure to cadmium oxide fumes in humans. One estimate is that 5 mg/m^3 can be considered lethal for exposure to cadmium oxide fumes over an 8-hour period. A 0.5 mg/m^3 exposure for eight hours results in clinical symptoms such as pneumonitis(La77,WHO80).

Several cases of cadmium oxide induced acute pneumonitis, which is sometimes fatal, are reported in the world literature each year. Most commonly these result from welders who are inadequately informed about appropriate preventive measures(La78).

Cadmium dust has produced acute respiratory toxicity but is considered much less severe than that caused by cadmium oxide fumes. No information is available on how much cadmium dust might prove to be lethal, but by extrapolation from animal studies a lethal concentration value of about 17 mg/m^3 for eight hours exposure has been suggested(Le72).

10.4 Chronic Toxicity

Low level long-term exposure of workers to cadmium has produced renal and pulmonary damage. Relatively intense exposures tend to produce more lung damage whereas lower exposures will tend only to show renal damage. A few reports suggest cadmium may affect the bone, liver and cardiovascular system. Some data indicates cadmium may be a carcinogen, but this is controversial.

Emphysema is the most commonly reported pulmonary effect caused by long-term inhalation of cadmium or cadmium-oxide fumes(Fr74,Ba52,Ad69). Other studies have indicated an impaired lung function and mild obstructive lung disease(Fr50,Fr48,Ka63).

Several studies indicate that the kidney is the target organ for long-term low level exposure(Fr74,No76). Reports suggest that damage to the kidney cortex occurs when tissue levels accumulate to between 200 and 300 mg Cd per kg of tissue(La77,No76, WHO80). The first reports of renal damage caused by occupational exposure to cadmium oxide came from Sweden(Fr48). Workers in an alkaline battery, nickel-cadmium factory showed proteinuria after exposure for more than eight years. Studies in similar production facilities in other countries showed a high incidence of proteinuria in cadmium workers(Ad69,Fr50,Ka63). Proteinuria is caused by damage to the proximal tubules in the kidneys.

Swedish cadmium workers exposed for more than 15 years often suffered from renal stones. Analysis of the stones showed they were essentially calcium phosphate. This suggests that cadmium interferes with calcium reabsorption(Fr50).

Reports from Britain and France indicate bone changes in workers chronically exposed to cadmium(Po65,Ni42). These changes involve a progressive weakening and softening of the bone. This condition is called osteomalacia and is characterized by brittleness of the bones.

Several reports have suggested that cadmium kidney damage causes an increased excretion of calcium phosphate such that calcium is lost from bone tissue(Ad69,Ka79).

Injection of cadmium into animals produces sarcomas at the injection site(Ch85). Rats exposed continuously for 18 months to an aerosol of cadmium chloride showed a high incidence of lung cancer. Of 120 male Wistar rats the high dose group received 50 ug Cd/m^3 71.4% developed lung carcinomas. The group receiving 25.6 ug Cd/m^3 showed a 52.6% carcinoma rate and the 12.5 ug Cd/m^3 showed a 15.4% carcinoma rate. None of the controls developed lung carcinomas(Ta83).

Up to this point, epidemiology studies of exposed workers have only produced limited and controversial data suggesting an association between cadmium exposure and carcinogenicity(Ki67,Po65,So82). However, in 1976 the

International Agency for Research on Cancer (IARC) convened a working group to evaluate the carcinogenic risk of cadmium to man. It concluded:

> "...available studies indicate that occupational exposure to cadmium in some form (possibly the oxide) increases the risk of prostatic cancer in man."(Ia76)

10.5 Rationale for Exposure Limit

For the purposes of standard setting for cadmium the health effects to be considered are:

1. Pulmonary edema (an acute effect).
2. Proteinuria as a marker of kidney damage (a chronic effect).
3. Possible carcinogenicity (a chronic effect).

Most Canadian jurisdictions follow the values adopted by ACGIH for cadmium exposures in the workplace (Table 1). In 1985 the Ontario Ministry of Labour commissioned a consultants report on the health effects of cadmium(Ch85). This suggests that cadmium will become a designated substance in the near future.

Since the IARC report in 1976, scientific opinion seems to have shifted somewhat. Investigations by Piscator(Pi79) indicate a strong link between prostatic cancer and dietary factors. It is now thought that cadmium is probably not directly involved in the etiology of prostatic cancer, but that substantial body burdens may have a promoting effect(Ha81).

ACGIH recommends that cadmium dusts and salts do not exceed 0.05 mg/m^3 and that cadmium oxide fume shall have a ceiling limit of 0.05 mg/m^3. An earlier designation to the suspected carcinogen category (A2) has been removed.

In its documentation, the ACGIH cites a number of reports demonstrating chronic cadmium toxicity at levels of around 0.1 mg/m^3 (Ha47,Ts67), but they take pains to point out the deficiencies of these retrospective studies. They state:

> "As is common with all reports of retrospective studies there is a tendency to ascribe present responses to present environmental levels with only slight, if any, recognition that gross overexposures occurred in the past prior to the installation of improved industrial hygiene controls."

They go on to emphasize that new cases of chronic poisoning in cadmium production workers can be attributed to:

> "...the continuing toxic effects from those gross overexposures prior to the installation of proper industrial hygiene control systems."

NIOSH recommends a TWA of 0.04 mg/m^3 with a 15 minute STEL of 0.2 mg/m^3 for cadmium dust and oxide fumes. This is apparently based on papers published by Lauwerys et al(La45,Ma75A). These authors cited a workplace limit of 0.05 mg/m^3 based on negative findings in workers exposed to 0.031 mg/m^3 but with proteinuria and reduced pulmonary function in workers exposed up to 40 years at 0.066 mg/m^3. The TWA exposure limit recommended by NIOSH seems to have a slightly better margin of safety than the ACGIH recommendation.

With respect to the possible carcinogenicity of cadmium ACGIH came to no conclusion and was content to refer to the NIOSH report which found the evidence contradictory.

It seems that in both the NIOSH and the ACGIH reports, the TLV for cadmium is designed to prevent proteinuria, pulmonary edema, emphysema and reduced lung function. There is no indication that the TWA levels reflect any concern about possible cadmium carcinogenicity. Indeed, ACGIH has now removed cadmium from the A2 category of suspected carcinogens.

In the consultants report on the health effects of cadmium, that was prepared for the Ontario Ministry of Labour, a calculation was presented to estimate the airborne levels of cadmium which might produce a critical concentration in the human kidney. It suggests that the Ministry of Labour might use an airborne exposure value for cadmium which takes into account a critical kidney concentration. This approach parallels that taken in the standard setting process for the toxicity of uranium as detailed in ICRP 26.

11.0 INORGANIC MERCURY

11.1 Occupational Exposure

The greatest potential for worker exposure to mercury seems to exist in the thousands of small workplaces that are involved in precision instrument repair. Significant potential for exposure also occurs in dentists offices. The large scale industrial use of mercury has declined in recent years due to changing technologies. Chlor-alkali plants that were used in the manufacture of chlorine gas and sodium hydroxide from sodium chloride were once the largest users of metallic mercury. These plants have largely switched their technologies and no longer use mercury electrode systems. The use of mercury in hospital and scientific instruments such as "silent switches", barometers, high precision thermometers and so on, is decreasing because of a replacement of these instruments with ones using solid state electronics.

11.2 Intake and Elimination

The major route of occupational exposure is inhalation. Mercury metal can exist as a colourless, odourless vapour at room temperature and approximately 80% of that which is inhaled is absorbed into the body(Go73).

Some metallic mercury can be taken into the body by skin absorption(Go73). Water-soluble mercury salts can also enter this way(Ch77).

Once inside the body mercury and its inorganic mercurous salts are oxidized by liver enzymes to mecuric mercury which is then excreted in the urine. Levels of mercury in urine are often used to monitor worker exposure to mercury. Small amounts are excreted in feces, sweat, saliva, exhaled breath, hair, nails and skin.

Mercury may temporarily accumulate in the kidney.

11.3 Acute Toxicity

Inhalation of high levels of mercury vapour produces symptoms of cough, shortness of breath, chest pains, and in severe cases, bronchitis or pneumonia. In addition, acute toxicity

may be marked by inflammation of the mouth with excessive salivation, tremor of the limbs, "drunken bahaviour", abdominal pain and vomiting. There may be acute kidney inflammation and death can occur within two weeks.

11.4 Chronic Toxicity

Repeated exposure to mercury over a period of time produces a chronic form of poisoning known as mercurialism. The disease presents with damage to the central nevous system, kidneys and the mouth.

Central nervous system damage causes tremor. There is trembling in the fingers, lips, eyelids, and tongue. The tremor may progress to produce jerking movements of the limbs.

A personality disorder called erethism develops and is characterized by an abnormal state of excitement or irritation. In severe cases, there is manic depressive psychosis and hallucinations.

High concentrations of mercury in the kidney causes proteinuria. In severe chronic poisoning kidney failure results.

Chronic mercury poisoning produces inflammation of the gums which may be accompanied by loss of teeth. There is inflammation of the mouth and excessive salivation.

11.5 Rationale for Exposure Limit

The health effects of overexposure to mercury can be summarized as follows:

1. Central nervous system damage producing tremor and 'drunkeness' (an acute effect).
2. Renal failure (an acute or chronic effect).
3. Central nervous system damage producing tremor and erethism (a chronic effect).
4. Damage to the mouth (a chronic effect).

The acute effects occur only at high exposures. Workplace limits have focused on the prevention of chronic effects.

In most Canadian jurisdictions the level for inorganic mercury exposure is the same as that specified by ACGIH (Table 1). ACGIH has two time-weighted average recommendations for inorganic mercury. Mercury existing as mercury vapour has a TWA of 0.05 mg/m^3. Mercury existing as inorganic salts has a TWA of 0.1 mg/m^3.

In Ontario, mercury is a designated substance with a time-weighted average of 0.05 mg/m^3.

The study by Smith et al was used to establish the limit of 0.05 mg/m^3. This study reviewed the health status of 567 workers exposed to mercury at 21 chlor-alkali plants operating in Canada and the United States(Sm70). Standard methods were used to measure and calculate TWA concentrations in workplace air and standard medical procedures were used for medical examination of workers. The findings for 567 workers were compared with those of a control group of 313 unexposed workers. Table 3 shows that the TWA concentrations in air were found to range between 0.01 and 0.27 mg/m^3. Approximately 85% of the workers were exposed to average concentrations less than 0.10 mg/m^3. There was no kidney damage in this population. Workers exposed to mercury levels in the air of 0.24 to 0.27 mg/m^3 showed symptoms consistent with early mercury intoxication such as tremor, nervousness and insomnia. These symptoms were also evident but to a lesser degree in workers exposed to 0.11-0.14 mg/m^3. Smith concluded that only workers exposed to mercury levels greater than 0.1 were at risk of developing signs of mercury intoxication. NIOSH proposed the TWA limit for mercury in air to be 0.05 mg/m^3 because it would provide a good margin of safety for most workers(Ni73). ACGIH presumably considered airborne levels of mercury vapour required a safety factor and followed the NIOSH lead in its recommendation of 0.05 mg/m^3. For some unexplained reason, it did not consider that inorganic mercury salts posed as much of a problem and recommended a higher value of 0.1 mg/m^3 for these. There is clearly no safety factor associated with this recommended level and a number of studies have indicated workers may be affected by exposure to concentrations of between 0.05 and 0.1 mg/m^3 (Sm48,Bi51,Tu56,La73).

ACGIH explains its 0.1 mg/m^3 recommendations by citing research indicating that very little mercury is deposited in the brain following absorption of mercury salts. Mercury vapour on the other hand deposits a relatively high percentage of absorbed mercury in the brain(Be69,Ma68). This research is also quoted by WHO. The WHO working group endorses the concept of a higher TLV for inorganic mercury compounds than for mercury vapour(WHO76).

12.0 COBALT

12.1 Occupational Exposure

Cobalt is a relatively rare metal and is produced primarily as a by-product of the mining and refining of other metal ores, chiefly copper. Exposure to cobalt occurs in mining operations and during its use in the production of high temperature alloys such as tungsten carbide. Cobalt is also used in the manufacture of permanent magnets. Cobalt salts are used as paint pigments and as catalysts.

12.2 Intake and Elimination

In industry the most significant route of cobalt intake in industry is through the inhalation of cobalt dusts. However, greater than 80% is probably eliminated by excretion in the urine.

12.3 Acute Toxicity

There is little information on the acute toxicity of cobalt by inhalation or skin contact. Ingestion of cobalt salts through the overzealous therapeutic administration of cobalt containing pharmaceuticals has produced vomiting, diarrhea and a condition known as polycythemia. Such effects have not been reported in industrial exposures.

12.4 Chronic Toxicity

Two types of lung disease have been reported in the tungsten carbide industry; an interstitial fibrotic process and an obstuctive airways syndrome(Mo75). The fibrotic condition can develop over a period of ten or more years and presents with symptoms of cough, shortness of breath and reduced pulmonary function(Co71).

The obstructive airways syndrome appears to be an allergic response and is characterized by wheezing, cough and shortness of breath while at work(Mo75,Co71). There is no indication that this disease progresses to the interstitial fibrosis. The condition does not develop until 6 to 18 months of exposure(Co73).

Skin contact with cobalt and its compounds produces an allergic dermatitis which usually occurs in areas subjected to friction such as the elbow, the neck and the ankles.

12.5 Rationale for Exposure Limit

The consequences of occupational overexposure to cobalt can be summarized as:

1. Lung fibrosis.
2. Obstructive airways disease (an allergic response).
3. Dermatitis.

All the above conditions are caused by prolonged exposure.

In most Canadian jurisdictions the recommended exposure limit is 0.05 mg/m^3 as a time-weighted average (Table 1). This is the value suggested by ACGIH. A STEL limit of 0.1 mg/m^3 is also suggested.

The ACGIH documentation on the TLV for cobalt is fairly concise. They note that studies of an industrial plant showed airborne cobalt to be ubiquitous and had probably been responsible for several fatalities over the years of operation. Exposures were in the order of 1 to 2 mg/m^3 (Fa59,Fa47).

ACGIH also reports that airborne dust samples collected by the Michigan Department of Health in 1946 showed high levels of 14.42 mg/m^3 but by 1964 these levels had been reduced to 1.5 mg/m^3. In 1966 ACGIH set the TLV at 0.1 mg/m^3 because:

> "...a limit of 0.1 mg/m^3 of Co metal fume and dust can be achieved without undue economic or technical difficulty and apparently was protective against hypersensitivity reactions." (Emphasis added.)

The reduction of the time-weighted average to its present level did not occur until after the publication of a report by Kerfoot et al(Ke75) who studied mini-swine exposed by inhalation to Co metal dust. After only three months of exposure the animals showed the early appearance of pulmonary disease at the then TLV level of 0.1 mg/m^3. There was a marked decrease in lung compliance and an increase in the amount of collagen (fibrous tissue) in the central areas of the lungs. Some of the mini-swine developed symptoms similar to hypersensitivity during the fourth week of exposure.

The TLV committee report:

> "...in view of the serious nature of these findings obtained after relatively short exposure period at the TLV of 0.1 mg/m^3 the recommendation to lower the TLV to 0.05 mg/m^3 as a time-weighted average is made, with a STEL of 0.1 mg/m^3. This recommendation is still under review by the committee."

No NIOSH recommendation for exposure to cobalt could be located.

13.0 NITROGLYCEROL (NG) AND ETHYLENE GLYCEROL DINITRATE (EGDN)

13.1 Occupational Exposure

NG is used to make dynamite, gun powder and rocket propellants. It is also used as a therauptic agent primarily in the treatment of pain caused by angina. EGDN is used only in the manufacture of dynamite. It is mixed in a ratio of about 8 parts with two parts of nitroglycerol.

Workers involved in the use or manufacture of explosives and in the manufacture of NG as a therauptic agent are at risk.

13.2 Intake and Elimination

The major route of exposure for workers who have direct contact with NG or EGDN is absorption through the skin. Workers who handle dynamite sticks for use in blasting also show some skin absorption. Blasting produces NG and EGDN dust in the air and significant amounts may be inhaled.

NG and EGDN are eliminated from the body by metabolism in the liver and excretion in the urine.

13.3 Acute Toxicity

Sudden exposure to NG or EGDN causes dramatic dilation of the blood vessels which results in intense throbbing headaches, skin flushing, dizziness, nausea and heart palpitations. These symptoms disappear over a period of two days if there is no further exposure. If exposure continues, symptoms last as long as a week but eventually disappear.

13.4 Chronic Toxicity

Workers with prolonged exposure to NG or EGDN develop spasms of the coronary artery that may lead to angina or sudden death. Chronic toxicity due to NG exposure was first documented by Laws in 1910(La10). He observed that nitroglycerol workers employed for many years would show an increase in the "area of heart dullness" and would be troubled with shortness of breath and irregular heart beat on exertion.

The first reports of what has become known as "Monday Morning Angina" or "Monday Morning Death" were published in the 1950s(Ba54,Sy52). One of these articles described three cases of sudden death without any apparent cause in men who made or filled cartridges with NG:EGDN dynamite in the Saar (West Germany). All three workers died suddenly on Monday or Tuesday morning and the only autopsy finding was a distension of the cerebral blood vessels.

These initial publications stimulated further reports from around the world concerning sudden death in dynamite workers.

The mechanism by which NG and EGDN produce chronic effects on the cardiovascular system is not understood, but there are some clues. It is thought that the heart adapts to the daily exposure and to the vasodilation effects which are induced. Because of vasodilation, the heart does not have to work or pump so hard in order to receive an adequate oxygen supply. When exposure to NG or EGDN ceases at weekends, the heart is stressed. As the blood vessels constrict the heart is forced to pump harder in order to receive sufficient oxygen.

This is undoubtedly an oversimplification of the events occurring at the physiological level. Unfortunately, animal experiments have yielded conflicting data about the chronic toxicity mechanism. Recently, it was reported that electrocardiographic data have shown abnormalities in patients undergoing withdrawl from nitroglycerol therapy for angina. The suggestion has been made that in dynamite workers the so-called Monday Morning Death represents a "pathological withdrawl syndrome"(Syd84).

13.5 Rationale for Exposure Limit

For the purposes of standard setting for NG and EGDN the health effects to be considered are:

1. Vasodilation resulting in headaches and skin flushing (acute effects).
2. Withdrawl syndrome (chronic effects).

In many Canadian jurisdictions the TLV-TWA for NG and EGDN is 0.05 ppm (Table 1). This level is the level recommended by ACGIH.

The ACGIH documentation traces the development of the current standard from 1962 when an original TLV of 0.5 ppm was recommended, despite earlier reports of severe headaches at this level(Mc46,El59).

In their 1966 documentation NG was combined with EGDN and a TLV for both substances alone or in combination was set at a ceiling value of 0.2 ppm.

In 1966 the ACGIH committee stated:

> "...the present TLV for nitroglycerol and EGDN is divided into two parts. The limit for intermittent exposure is 0.02 ppm, based on the findings of Trainor and Jones(Tr66) that volunteers exposed to mixtures of these two nitrates showed immediate falls in blood pressure and marked headaches at 2 mg/m^3 (between 0.1 and 0.2 ppm)."

The TLV committee also indicates that there are at least two reports in which sudden deaths have occurred in workers exposed to average concentrations in the 0.18 to 0.24 ppm of NG although additional exposure by skin absorption could not be ruled out in these cases(La72,OS71).

In 1966, then, there were two limits. The first was a TWA of 0.02 ppm for intermittent exposure. This represents a five-fold safety factor with respect to the studies of Trainor and Jones, but the time span of 'intermittent' was undefined. The second was an 0.2 ppm ceiling for continuous exposure and had no safety factor. Indeed it is a level at which dramatic physiological effects have occurred.

NIOSH considered that workplace exposure to nitroglycerol should be controlled to concentrations that will not cause vasodilation as indicted by throbbing headache and/or decreases in blood pressure(NI78). A 20 minute ceiling of 0.01 ppm (0.1 mg/m^3) for NG or for NG and EGDN combined is recommended. This implies at least a ten-fold safety factor.

Strangely, the ACGIH committee does not consider vasodilation, with concomitant headache, an important marker for possible long-term health effects. In its documentation it states:

> "Although not specifically stated as a policy, the committee has generally adopted TLVs which, if adhered to, will prevent pharmacologic effects in exposed workers. After a review of the literature the committee recommended a raise in the time-weighted average TLV from the 0.02 to 0.05 ppm in 1981".

This recommendation to raise the TLV to five times the value recommended by NIOSH rather than half it to concur with the NIOSH criteria is, according to ACGIH, based on analogy with a study of the effects of propylene glycol dinitrate(St74). In this study tolerance to headaches was reported after several repeated eight hour exposures at 0.22 ppm.

The stance of ACGIH on NG and EGDN is most incongrous with the available health effect data. According to their documentation, workers will, in the initial stages of exposure, not be protected against headache. Indeed they are apparently expected to endure throbbing headaches until such time as they develop tolerance.

Of greater concern is the view that headaches are of no importance in considering the possible long-term consequences of exposure. Clearly headaches, represent the early signs of vasodilation and reflect the beginning of the heart's "accomodation" to daily exposures to NG or EGDN. For ACGIH to ignore this probably means that significant political, economic or other considerations played a role in choosing the TLV-TWA.

14.0 SILICA

14.1 Occupational Exposure

The principal exposure to silica occurs in the mining industry where silica dust is generated during operations such as blasting, digging and drilling. These exposures are widespread since the ores of most metals, including copper, silver, gold, nickel, uranium are found in silica-containing rock. Exposure to silica also occurs in quarrying and construction industries.

In Ontario much silica exposure occurs in foundry operations using sand molding processes. Workers in pottery, porceline and enamel industries are also exposed(On82).

14.2 Intake and Elimination

Silica enters the body primarily through inhalation. Silica dusts contain particles with a wide range of shapes and sizes, but only a proportion of these particles are respirable. Of all particles inhaled, those with a diameter larger than about 10 um are removed in nasal passages and upper airways. Approximately 50% of the particles finer than 5 um in diameter penetrate further than the nose during normal breathing. Particles 0.5 um to 5 um in diameter are carried into the alveoli of the lungs and are deposited there under gravity. It is thought that the "ideal" size for deposition in the alveoli is a diameter of 2 um.

Some inhaled dust particles are permanently retained, but others can be cleared from the upper airways and from the alveoli. Calculations estimate that a miner may receive a dust load of around 1,000 grams during his working life time, but rarely are more than 30 grams of dust found at post mortem.

14.3 Acute Toxicity

Silica exposure can produce a condition known as acute silicosis. It is not acute in the sense that it develops immediately after the first exposure but it occurs in workers exposed to unusually high levels of free respirabable silica for periods ranging from a few weeks to four or five years. Up to 18 months may lapse from the time of the first exposure to the development of shortness of breath, fever and weight loss.

There is rapid progression of respiratory failure which can result in death within one or two years. Acute silicosis has been found to occur in sandblasting, rock drilling in tunnels and quarrys and in the manufacture of abrasives.

14.4 Chronic Toxicity

Repeated inhalation of silica dust over many years results in a progressive fibrosis of the lungs known as chronic silicosis. Chronic silicosis is similar to acute silicosis, but has a much longer latency period, usually ten years or more. Chronic silicosis is more commonly encountered than the acute form. Early symptoms are frequently non-specific. Symptoms may include cough and sputum, laboured or difficult breathing, wheezes and chest pain. The non-specific symptoms often delay an association between silica exposure and fibrotic lung. Even after removal from exposure, silicosis progresses and there is no effective treatment or cure(Mo75,Br76,Wa76). As the disease worsens chronic bronchitis, cyanosis, and emphysema may develop. Death may result due to cardiac or respiratory failure.

There is no indication that silicosis is associated with an increased risk of cancer of the respiratory or other systems.

14.5 Rationale for Exposure Limit

The health effects of overexposure to silica dust may be summarized as follows.

1. Acute silicosis (a subchronic effect).
2. 'Classical' silicosis (a chronic effect).

In most Canadian jurisdictions the current TLV-TWA is 0.1 mg/m^3 respirable dust (Table 1). This is the limit recommended by the ACGIH.

In Ontario, silica is a designated substance and according to the regulation respecting silica:

> "...the time-weighted average exposure of a worker to airborne silica should be reduced to the lowest practical level with a view to achieving at least 0.1 mg/m^3 silica of air by volume and in any event shall not exceed 0.2 mg/m^3 of air."

The documentation of ACGIH for crystalline silica is unique in that it consists of a description of the disease condition but does not attempt a review of the literature which might give clues to the origin of the 0.1 mg/m^3 limit.

NIOSH reviews a few very limited studies on the toxicity of crystalline silica and recommends an exposure limit of 15 u/m^3(Ni75). This is apparently based on the work of Theriault(Th74A,B,C) who indicated that people exposed to quartz concentrations of around 100 ug/m^3 experience annual decreases in pulmonary function greater than would occur due to aging alone.

A long-term follow-up study by Graham et al re-exaimed the work of Theriault and found that the lung function parameters measured had actually increased rather than decreased as suggested in the original studies(Gr81). In order to make the results as comparable as possible, Graham obtained the same respirometers that were used by Theriault et al in their investigations. Graham concluded that:

> "...technical deficiencies in the previous studies led to exaggerated and erroneous estimates of loss (of pulmonary function). At this time, the actual decrement in pulmonary function values for exposed granite workers is not known and requires further investigations. Because the newly proposed, stricter standard for silica was importantly influenced by the previous studies, we believe the adoption of this standard would be premature."

Graham noted a leak in the respirometer used by Theriault and suggested that this accounted for the large discrepancy in results(On82).

On the basis of the Graham study, NIOSH has begun to reevaluate all its technical data relating to silica exposure and its proposed limit of 15 ug/m^3. This evaluation process is still underway and results will not be known for some time.

In its report on the designation of silica in Ontario, the Ministry of Labour is equally perfunctory in its treatment of the basis for the 0.1 mg/m^3 limit. It discusses a few animal investigations that largely relate to the size of silica particles that may be active in producing fibrosis, but does not cite any investigations on the dose response relation.

Epidemiology studies are mentioned but are dismissed because most of them have not attempted to correlate specific exposure levels to the observed incidence of silicosis. There is no evidence that a threshold of exposure for silicosis exists. On the matter of dose response relation, the MOL report states that:

> "...it appears that the higher the concentration of free silica inhaled, the more rapid the development of silicosis. It is also apparent that as dust is controlled the incidence of silicosis decreases, the severity of the disease lessens, and the length of time for the disease to become apparent increases. Although these general trends are clearly established, the following features of silica exposure and silicosis make it difficult to establish accurate dose response relationships:
>
> - the gradual onset and long latency period of silicosis;
> - non-specific symptoms of silicosis;
> - lack of sensitivity in diagnostic measures;
> - questionability and validity of extrapolating animal and tissue study results to humans;
> - problems in air sampling methodology;
> - inherent weaknesses of the available epidemiological studies;
> - lack of specific data on dose response relationships in Ontario silica exposure industries."

The Ontario Worker's Compensation Board has compiled statistics on silicosis since 1928. The analysis of these statistics is a complex task since the criteria for determining a work-induced silicotic conditions has changed several times over the years.

According to the WCB statistics, the incidence of silicosis in Ontario has declined from about three per one-thousand men in 1930-34 to two per one-thousand men in the period 1935-48. From 1949 to 1956 the rate is about one per one-thousand, but between 1957 to 1974 the rate fluctuated between 0.5 and 1.5 per one-thousand. It is speculated that uranium mining, which began in Ontario in 1954, was responsible for increases noted in 1965 to 1973.

The data presented by the above three standard setting organizations indicate that despite the long history and incidence of silicosis, the animal and human research data are

wholely inadequate to provide a basis for an exposure limit recommendation. The value of 0.1 mg/m^3 which has been recommended by most standard setting organizations, seems to be an abritary figure based on the general rule that decreased incidence occurs through decreased exposure.

If the Ontario statistics are representative of actual disease occurrence at the 0.1 mg/m^3 level, then it appears that a 0.1% incidence of silicosis is considered acceptable by standard setting authorities.

15.0 VINYL CHLORIDE

15.1 Occupational Exposure

At normal temperatures and pressures vinyl chloride is a gas. Occupational exposure can occur during its manufacture. Large quantities of vinyl chloride are used in the plastics industry and exposure occurs during the manufacture of PVC.

In Ontario, there is one large producer of vinyl chloride and two large producers of PVC plastic products. In addition, there are many much smaller fabrication plants which use the PVC end product in their manufacturing processes. Some workers in these smaller plastic product manufacturing operations have the potential for exposure to vinyl chloride which is present in the PVC resin.

15.2 Intake and Elimination

The main route of exposure to vinyl chloride in the workplace is through inhalation. Inhaled vinyl chloride passes through the lungs and is metabolized by the liver. At least two biochemical pathways and a number of end product metabolites have been identified in rats(Ia79). Excretion of the metabolites occurs in the urine.

15.3 Acute Toxicity

Short exposure to high concentrations produces sleepiness, drowsiness, euphoria, a feeling of drunkenness and in extreme cases death. These are all symptoms of central nervous system depression. Two cases of accidental death due to exposure to high concentrations were reported in Ontario in 1958 and 1959(On81).

15.4 Chronic Toxicity

A variety of chronic diseases have been reported.

Vinyl Chloride Disease (Acro-Osteolysis) produces a clubbing of the ends of the fingers and hardening and swelling of fibrous tissue of the skin. The bones at the ends of fingers degenerate. Some workers experience Raynaud's syndrome which

is a cold induced, sudden palor of the fingers. In some instances, decalcification of the knee caps, rheumatoid pain and cysts in the hip joints have developed(Le74).

Signs of this disease were first reported in Russian and Romanian workers during the 1950s. It appeared largely in reactor cleaners who were exposed to high concentrations of vinyl chloride(On81).

Vinyl chloride induced disturbances in the immune system are thought to cause the disease(War76).

Some workers exposed to vinyl chloride have shown abnormal chest x-rays(Li75). Other studies have shown increases in obstructive lung disease in workers exposed to both vinyl chloride in polyvinyl chloride (PVC) dust(Mi75).

Liver function studies in exposed workers show a variety of abnormalities. Various types of liver fibrosis can be identified together with cell transformations suggesting early stages of cancer.

The primary health concern with vinyl chloride is its potential to cause cancer. Prior to 1974 the primary hazard of occupational exposure to vinyl chloride was considered to be due to its anesthetic and explosive properties(Hy80). Even at that time reports had suggested that vinyl chloride induces tumours in rats (Vi70). In January 1974 the B F Goodrich plant in Kentucky reported to NIOSH that a rare liver tumour, angiosarcoma, had been found in three of its workers(Cr74). Similar reports from other countries confirmed an unusual predominance of this rare liver condition in workers exposed to vinyl chloride. In 1978 a Canadian study listed ten cases of angiosarcoma in the livers of workers from one plant in Quebec(De78).

While a definite cause-effect relationship has been established for angiosarcoma of the liver, a dose-response relationship has not. Most workers who developed tumours were exposed during a period when vinyl chloride levels in PVC manufacturing plants were not controlled. Levels were probably several hundred parts per million, many times the present allowable limit.

Some studies have suggested that vinyl chloride may also be responsible for tumours of the lungs, brain and lymphatic system(Du76,Vo79). These studies have not been substantiated.

15.5 Rationale for Exposure Limit

The major health concerns of overexposure to vinyl chloride can be summarized as:

1. Central nervous system depression (an acute effect).
2. Angiosarcoma (a chronic effect).
3. Acro-osteolysis (a chronic effect).

Most Canadian jurisdictions have adopted (Table 1) the TLV-TWA of 5 ppm which is the level recommended by ACGIH. ACGIH also gives vinyl chloride an Ala classification, meaning that it is a recognized human carcinogen.

In Ontario vinyl chloride is a designated substance with a time-weighted average exposure which must not exceed 2 ppm. An excursion limit maximum of 10 ppm is also specified. The excursion limit must be included as a part of the time-weighted average.

In its documentation ACGIH mentions that at one time, vinyl chloride was thought to be so low in toxicity that it was considered for use as a surgical anesthetic. For a time, it was used in vetrinary practices, but was discontinued because of its flammability, poor efficacy and its ability to cause cardiac irregularities at anesthetic concentrations(Do86).

The documentation indicates that animal studies on the acute inhalation toxicity of vinyl chloride were carried out as a consequence of two deaths in Canada(Ma60). In these studies inhalation of 10, 20 and 30 volume per cent vinyl chloride produced deaths due to narcosis only at the highest level in mice, rats and guinea pigs. Further details in the documentation describe acute inhalation toxicity experiments, all of which lead investigators to consider vinyl chloride to be very low in toxicity and to recommend exposure levels for workplaces in the 100's of parts per million. Prior to 1974, ACGIH recommended a time-weighted average for vinyl chloride of 200 ppm with a 500 ppm ceiling.

The report by the B F Goodrich company to NIOSH on January 22-23rd, 1974 clearly had a marked impact and produced a flood of animal toxicity and epidemiology studies. To date, estimates of between 70 and 100 angiosarcoma cases have been reported world wide as a result of exposure to vinyl chloride.

ACGIH concentrates on animal toxicity and epidemiology studies where levels of vinyl chloride were several hundred or even several thousand ppm. The documentation does not report the consequences of low level exposure to vinyl chloride presumably because of the the absence of any data. Despite this ACGIH states in their documentation:

> "It is the judgement of the committee that if the average exposure to vinyl chloride does not exceed 5 ppm, there will be no increase in the incidence of cancer, specifically of angiosarcoma of the liver. It is probable that the cancers reported and attributed to vinyl chloride among PVC workers resulted from exposure many times this level."

At this point, it is worthwhile recalling the statement on carcinogens made by ACGIH in its TLV booklet. They remark that for assigning an industrial air limit an approximate threshold of neoplastic response must be determined so that an appropriate risk or safety factor can be applied. Yet, throughout their documentation on vinyl chloride their is no indication of what they consider the appropriate threshold to be.

NIOSH reviews the same literature as ACGIH, but its philosophy is different. In the absence of any proven threshold limit for carcinogens generally, and vinyl chloride in particular, NIOSH seems to prefer to recommend the "lowest detectable level". For vinyl chloride NIOSH has recommended a level of 1 ppm as a time-weighted average with a ceiling of 5 ppm. It is evident from the NIOSH recommended standard(Ni74) that the reviewers considered 1 ppm to be the lowest detectable level. This is an error. The lowest detectable level is around 0.02 ppm.

A refreshingly different approach was used by the Ontario MOL. They took the steps to calculate and derive, from animal data, an acceptable concentration for vinyl chloride. The level derived includes considerations of acceptable risk - an unusual approach in occupational health. In describing this calculation they state that:

> "...it has been assumed that no threshold exists; that the function is a linear one; that the effects observed at high doses can be extrapolated to lower doses in the same species; that if the chemical is inhaled it is possible to extrapolate directly from animal to man; that the risk to both animal and man is similar, if a similar fraction of their life is spent in a smaller exposure concentration; that the latent period for development of a specific

tumour takes the same fraction of both species life times if they have experienced similar exposures; an acceptable risk has been taken to be 5×10^{-4} per year. Based on the animal data and recognizing fully the assumptions that have been made, it has been calculated that an acceptable concentration for vinyl chloride for the air in the workplace is 2 ppm."

The MOL used a calculation to determine risk at the no effect level. The no effect level is the highest concentration at which no excess tumour risk was discernable. The purpose of this method was to obtain the smallest risk factor compatible with the data in a single exposure group. The groups chosen were Sprague Dawley rats exposed for 52 weeks to levels of 50, 250, 500, 2,500, 6,000 and 10,000 ppm vinyl chloride(Ma75).

They assumed that the excess tumour risk corresponding to vinyl chloride concentrations "C" was less than the risk "R" calculated using the following formula:

$$R = \frac{RO \times C}{CO}$$

WHERE: RO = the upper confidence limit of the excess tumour risk corresponding to vinyl chloride concentration CO

CO = the highest vinyl chloride concentration at which no excess tumour risk was discernable (no effect level).

Excess tumour risk was the fraction of exposed animals which developed the tumour during the experiment less the fraction of unexposed animals which developed the tumour during the experiment. The upper 99% confidence limits of excess tumour risk were used.

The factors "RO/CO" were calculated when the tumour frequences in control animals and all exposed animals was statistically significantly different.

The excess risk factors calculated using this formula are presented in Table 4.

In order to obtain the risk factors for humans it was assumed that the lifetime tumour risks were the same in man and the Sprague Dawley rats when the same fraction of each species average life time was spent exposed to the same concentration

of vinyl chloride in air. In this calculation the average life time was taken to be two years and the fraction of the average life time spent in exposure by the Sprague Dawley rat was calculated to be:

$$\frac{4 \text{ hours/day} \times 5 \text{ days/week} \times 52 \text{ weeks}}{24 \text{ hours/day} \times 7 \text{ days/week} \times 104 \text{ weeks}} = 6.0 \times 10^{-2}$$

The excess tumour risk factor when the duration of exposure was an averge life time was calculated to be:

$$\frac{4.3 \times 10^{-3}}{6.0 \times 10^{-2}} = 7.2 \times 10^{-2} \text{ per ppm vinyl chloride in air}$$

Where 4.3×10^{-3} is the upper confidence limit on excess risk per ppm derived from data on the incidence of all tumours in Sprague-Dawley rats (Table 4).

The annual exposure duration for a worker was assumed to be 8 hours per day, 5 days per week, 52 weeks and the average worker's life time was taken to be 70 years. The fraction of the average life time spent in exposure during the course of one working year was calculated as;

$$\frac{8 \text{ hours/day} \times 5 \text{ days/week} \times 52 \text{ weeks}}{24 \text{ hours/day} \times 7 \text{ days/week} \times 52 \text{ weeks/year} \times 70 \text{ years}} = 3.4 \times 10^{-3}$$

Hence, the life time risk when the exposure is 3.4×10^{-3} of an average life time was calculated to be:

$$3.4 \times 10^{-3} \times 7.2 \times 10^{-2} \text{ per ppm} = 2.4 \times 10^{-4} \text{ per ppm}$$

The report concluded that the annual excess tumour risk for persons who are continually exposed to 1 ppm of vinyl chloride will increase towards a maximum value of 2.4×10^{-4} per person or 24 excess tumours per year amongst 100,000 workers.

The annual acceptable risk for a worker was obtained by using the data of the International Commission on Radiological Protection(Ri77) and was calculated to be 5×10^{-4} or 50 excess deaths per year among 100,000 workers.

Based on the above calculations and assumptions the workplace exposure limit was set at 2 ppm.

The approach used by the Ontario Ministry of Labour is significant in two respects.

1. It attempts to carry out a risk assessment based on animal data as a part of the standard setting procedure. There is no pubished evidence to suggest that ACGIH or NIOSH have attempted such approaches.

2. It is the first instance in which an acceptable risk of chemical exposure has been related to the risk system developed for radiological protection. Indeed the concept of acceptable risk is rarely used in occupational health.

Perhaps even more remarkable about this exposure standard is that labour and public interest groups were apparently prepared to accept a numerical risk. It is possible that all parties involved recognized the very empirical nature of the calculations. No vinyl chloride induced angiosarcoma has ever been reported in Ontario. Given that probably less than 100 such cases have been reported world-wide it seems plausible that the calculation greatly overstates the risk from exposure to 2 ppm.

16.0 SUMMARY OF THE RATIONALES USED IN ESTABLISHING TLVs FOR CHEMICALS

Table 5 summarizes the major factors which have formed the basis for establishing TLVs of the ten chemicals discussed in this report.

Human health data sometimes compromised by economic considerations has been used in at least eight out of the ten chemicals.

With respect to the human health effects, at least four different concepts emerge in the judgement process:

1. Assignment of a standard which ACGIH believes produces only 'minor' injury in a proportion of exposed workmen (TDI, NG).
2. Assignment of a standard which the committee believes no illness will be caused during a lifetime of exposure (mercury, n-hexane, NG, cadmium and cobalt).
3. Assignment of a standard on the basis of comfort from irritation or objectionable odour (hydrogen fluoride).
4. Assignments made the basis that some fatal disease will occur at an 'acceptable' risk level (silica, vinyl chloride (Ontario MOL)).

These concepts clearly embody quite distinct criteria for judging the acceptability of a health effect. It is evident that which criteria apply to which chemical is a judgemental value reflecting to a considerable degree individual perceptions on the definition of health.

Animal data forms the basis for the figures derived and used for cobalt and vinyl chloride. In these two instances, there was a direct extrapolation from animal to man with no apparent attempt to allow for differences in metabolism, body weight or other variables. Only in the case of vinyl chloride was there an allowance made for life span differences.

Only three of the ten chemicals reviewed, namely n-hexane, cadmium and mercury vapour show any indication of a safety factor in the limit. It is interesting to note that with these three the economic or technical feasibility of reaching the recommended set level was not mentioned in the ACGIH documentation.

17.0 HISTORY OF EXPOSURE LIMITS FOR WORKPLACE RADIATION

Ionizing radiation, in the form of x-rays, was discovered by William Konrad Roentgen in 1895. Roentgen observed that the rays could pass easily through paper and wood but not through metals or other dense materials. The potential uses of Roentgen's rays were quickly appreciated and added a new dimension in diagnostic medicine.

Early applications of x-rays used them to examine bone fractures and to detect foreign bodies in tissues. Rapid discoveries soon enabled x-rays to reveal details of the softer tissues of the body.

The earliest x-ray injury was reported by Grubbe(Gr49) and Edison(ED96). Both authors noted severe smarting of the eyes after several exposures to a discharge tube. Edison also reported loss of hair and skin reddening effects(Ed96). The skin reddening effect became the first reference point for determining dose and could be defined as that amount of ionizing radiation which causes skin erythema. This very crude measure of dose was called the skin erythemal dose (SED) or sometimes the threshold or minimal erythemal dose (TED or MED respectively).

Several studies with guinea pigs showed x-ray damage was not limited to the skin, but could also appear in body organs(Ro02).

These early demonstrations of biological harm raised concerns for the safety of patients and radiologists(Ro03). Early radiographic exposures used in medicine could take up to an hour and a half and skin burns on patients were a frequent result.

The development of radiation protection owes much to the concerns of early radiologists who sought to establish a maximum dose which could be tolerated continuously by the human body. However, at this time there was no international agreement on the quantities and units which would define the measurement of radiation. Consequently, no uniform description of radiation exposure could be made. A paper on protective devices, presented at a 1915 meeting of the British Roentgen Society, resulted in the adoption of the following resolution:

> "...that in view of the recent large increase in the number of Roentgen ray installations this Society considers it a matter of the greatest importance that personal safety of the operators conducting the Roengten ray examinations should be secured by the universial adoption of stringent rules and that the council of this Society be requested to meet at an early date to take steps to secure this."(Ka15)

In the subsequent years of the first world war, there was no further mention of radiation protection. Then, in 1920 there were a number of deaths from aplastic anemia in people who had worked with military medical services, and this stimulated further action on radiation protection. Groups in the United States and Britain adopted similar sets of protection recommendations, (Pr22,Re21,Ka26) which largely related to working conditions and shielding requirements. The limitations of these guidelines was appreciated and there was wide recognition that internationally accepted units of exposure should be defined.

The problem of units of exposure was addressed at the First International Congress of Radiology in 1925. This congress recommended the formation of a committee, the International Committee on Radiological Units (IRCU). This committee's task was to reach a consensus on radiological exposure units. Such consensus, was seen as a prerequisite to recommending a 'safe' dose level.

This "safe" dose level in radiology became known as the tolerance dose and it was seen to signify the amount of radiation which the tissue concerned was able to tolerate. Such a dose was not regarded as entirely harmless and tolerance doses could not be readministered indefinitely without effect.

Taylor(Ta71), in his book on radiation protection standards, notes that:

> "...general concepts of tolerance dose based somewhat on experience and somewhat on assumptions, dealt with a cause effect relationship which could not be positively proven or disproven. Precisely the same situation exists today, although currently our knowledge is much more extensive and that means measurement and definition are much more refined."

Tolerance dose eventually became known as permissible dose and was determined on the basis of whether or not effects could be observed at that level.

The first attempt to define permissible dose in terms of a numerical value was made by Mutscheller[Mu25]. He researched exposure patterns in a number of installations using ionizing radiation and noted that in a month members of staff received what was described as about one, one-hundredth of a threshold erythema dose. He considered the monthly work time to be around 200 hours and concluded that radiation should be harmless at this level. If there was no recovery from each exposure it would take 20,000 hours (about eight years of 8-hour days) to produce an erythema.

The application of Mutscheller's concept was limited, but in the absence of other systems, received modest acceptance. The permissible dose was calculated as one, one-hundredth of a skin erythemal dose. Following Mutscheller's lead, a number of other researchers calculated tolerance doses which showed remarkable similarity to that recommended by Mutscheller[Gl29,Be30,Ba28,Ch28].

By 1928, a meeting of the Second International Congress of Radiology in Stockholm adopted several previously detailed British proposals on shielding and working conditions to form the pattern for international recommendations in radiation protection.

Specifications for shielding included the requirement that it should not be possible for:

> "...a well-rested eye of normal acuity to detect, in the dark, appreciable fluorescence of a screen placed in the permanent position of the operator."

Since, at this time, there was no suitable means to measure radiation, none of the specifications referred to doses or exposures or specific distances between radiation sources and the operator, but they did suggest that the operator be as far away from the source as possible. Most of the recommendations consisted of detailing specific thicknesses of lead which were necessary to shield against radiations produced at given voltages for x-rays or for given quantities of radium. However, progress was made in the tentative adoption of the Roentgen as the international unit for ionizing radiation. This recommendation was made by the ICRU. The Roentgen had, by that time, already been in use for several years.

Following this international acceptance, there was a rapid consolidation of information and efforts leading to the conversion of dose measurements from skin erythema units to Roentgens. This set the stage for the future adoption of a tolerance dose by NCRP and ICRP.

The 1928 Congress also saw the birth of a new committee, the International X-Ray and Radiation Protection Committee (ICRP), whose task was to develop and propose guidelines for radiation protection.

By 1934 this committee had reviewed the early work of Mutscheller and others and proposed an exposure limit of 0.2 R per day. In the same year, the U.S. radiation protection body, the National Council of Radiation Protection (NCRP) recommended 0.1 R per day for a 7-hour, 5-day workweek. A standard of 0.2 R per day was adopted by the International Committee on X-Ray and Radium Protection (ICRP) in 1934. The difference in these standards came about because each group used a slightly different rounding procedure(Ta80).

It is interesting to note that the recommendations of the ICRP were based on the absence of any kind of observable effect.

No biomedical discussion or reports were presented in explanation of the value adopted. ICRP was content to state:

> "...the evidence available at present appears to suggest that under satisfactory working conditions a person in normal health can tolerate exposure to x-rays to an extent of about 0.2 international Roentgens (R) per day of continuous radiation. On the basis of continuous irradation during a working day of 7 hours this figure corresponds to a dosage rate of 10^{-5} R/sec. The protective values given in these recommendations are generally in harmony with this figure under average conditions. No similar tolerance dose is at present available in the case of radium gamma rays."

The final remark about gamma rays apparently reflected uncertainty as to the basic biological mechanism involved. The NCRP report stated:

> "...the safe general radiation to the whole body is taken as 1/10 R per day for hard x-rays and may be used as a guide in radium protection. 5 R per day has been taken as the tolerance for the fingers. It must be emphasized that the calculation of radium dosages is not easy, and too great a reliance is not to be put on the above figures."

Taylor adds:

> "...with respect to the last statement that it was not to question the value of tolerance level 1/10 R per day, but was to emphasize the fact that it was not then possible to control exposure by measurement means with very great accuracy. Because of this some additional rules of thumb guidance were provided."(Ta71)

These early recommendations obviously had little scientific substance to them and, in large part, were probably value judgements aided by "rules of thumb".

Much of the initiative and leadership developed by the ICRP was lost during the years of growing international tension prior to the second world war. However, the initial work of ICRP was continued in the United States by the NCRP. Lauriston Taylor, formally a member of the ICRP, and at the time employed with the U.S. National Bureau of Standards, was chairman of NCRP. He was a key figure in the development of radiological protection concepts and standards. Other members of NCRP represented the American Roentgen Ray Society, the Radiological Society of North America, the American Medical Association and x-ray equipment manufacturers.

During the 1930's, NCRP produced a number of reports dealing with aspects of x-ray protection, radium protection and injury to radium dial painters. The latter report provided valuable human data on the injurous effects of internal radiation.

Many of the follow-up studies on surviving radium dial painters were carried out by Evans and his collegues(Ev81). Evans reported that even by 1936 insufficient human cases had been studied to ensure a firm basis for a suggested permissible body burden of radium. He also noted that rat studies had not proved helpful since they demonstrated no osteogenic sarcomas until skeletal concentrations were already several hundred times that which were known to cause bone cancers in humans.

Evans states that:

> "...judgemental decisions (about permissible body burdens) had to be made on the basis of observations on man."

They chose a level of 0.1 u Ci as a body burden based on the observation of several persons with residual body burdens below 0.5 u Ci and no effects. The 0.1 u Ci level for 226 Ra was

officially adopted internationally by the early 1940s. The standard remains unchanged today. The 226 Ra standard is the only "true standard" for internal radiation. Other internal standards have been primarily based on data from external radiation exposures or have been derived by analogy with radium (e.g., the body burden for plutonium)(La73).

In the early 1940's, presumably because of the war effort, major research in radiation was directed towards the development of controlled fission and nuclear weapons. Much of this work was highly classified and became known as the Manhattan project. This intensive research expanded the use and applications of all kinds of radiations and radioactive materials. In turn, this increased usage necessitated a greater understanding of the need for control measures. Authorities in charge of the new applications for radiation were faced with the decision of what amount of radiation might be acceptable by the work force. In the early stages, they adopted the tolerance doses recommended by the NCRP. However, they felt somewhat uneasy about these levels since they had been arrived at on the basis of rather scant evidence. As a consequence, efforts were made to try and evaluate the recommended tolerance dose levels on a more quantitative basis. There was particular concern about the absence of data on the effects of two or three or more Roentgens per day for fairly extended periods.

Sizeable investigations were instituted at the U.S. National Cancer Institute, the University of Rochester, University of Chicago and Oakridge. At NCI, mice, guinea pigs and rabbits were exposed to gamma rays for 8 to 24 hours a day, 7 days a week at doses ranging from 0.11 to 8.8 Roentgens per day for the life time of the animals. At Rochester, rats, rabbits and dogs were exposed to x-rays for short daily periods, 6 days per week, at dose rates ranging from between 0.1 to 10 Roentgens per day. Similar studies were carried out in Chicago and Oakridge to compare the effects of gamma rays and neutrons.

There was little evidence of effect on the basis of observed skin damage but it was noted that irradiated animals did not survive as long as non-irradiated ones(St52). Experiments with animals showed that gamma rays, given chronically in the order of 10 roentgens per day, produced no opacity of the cornea nor cataract formation for even total doses as high as 12,000 Roentgens. On the other hand, acute doses as low as 400 Roentgens, applied at the time of birth, caused eye lesions in mice.

For chronic irradiation there was a significant reduction in the life span of animals exposed at doses around 0.5 R per day. Fertility was also studied and it was found that doses in the order of 1 R per day produced little if any change in average litter size, while doses of around 5 R per day delivered for long periods of time impaired fertility.

The results of these studies gave authorities of the time a degree of comfort about the use of a tolerance dose level of NCRP's 1/10 R per day.

In the light of studies on the genetic effects of ionizing radiation on fruit flys (Drosophila) there was special concern that similar effects might be noted in workers on the U.S. plutonium project. Experiments with mice carried out during this project exposed mice to dose rates of 0.1 to 10 R per day. Small effects were found at exposures of 100 R and it was felt there was an ample margin of safety if exposures were maintained below 50 R at a rate of 0.1 R per day.

The U.S. national program (the Manhattan project) produced vast amounts of research into the effects of radiation exposures. This intensive activity spawned a whole new discipline in protective science which came to be known as health physics.

By 1946 it was recognized that radiation use in all categories would be rapidly expanded and concerns about protection encompassed a much larger group of potential radiation workers. In some instances potential exposure of the general population was a concern. To meet this new demand NCRP convened its first post-war meeting in December 1946 and established sub-committees to report on the following:

1. Permissible external dose.
2. Permissible internal dose.
3. X-rays up to 2 MeV for heavy ionizing particles (neutrons, protons, and heavier particles).
4. Electrons, radium and gamma rays above 2 MeV.
5. Radioactive iostopes, fission products, including their handling and disposal.
6. Monitoring methods and instruments.

Reports on all these subjects were prepared and published by NCRP. There seems to have been much cooperation and exchange with the United Kingdom and Canada on the nature and concepts in these reports. These tripartite efforts apparently facilitated adoption of many of the recommendations of NCRP by the ICRP (now re-named International Commission on Radiological Protection) when it first reconvened in 1950.

Around this time, a new unit of dose, the Rad, was approved and recommended by ICRU. Some dosage values recommended in the various NCRP and ICRP reports were expressed in terms of the Rem. This unit was not yet officially recognized by the ICRU.

It is noteworthy that the ICRP in 1950 stated that it was not in a position to make firm recommendations regarding the maximum permissible amounts of radioactive isotopes that might be taken into or retained by the body. Whole body exposures were recommended at 0.5 R per week. This represented a 50% reduction from the 1.0 R/week previously recommended by the International Commission of X-ray and Radiological Protection. A further reduction to 0.3 R per week was recommended by ICRP in 1953. It is unclear from the literature why these reductions occurred, but they may have reflected the beginnings of the concept that any exposure involves some risk.

By 1955, this risk concept led to the first expression of what is today called the ALARA principle. ICRP supplement, number 6 stated:

> "...Whilst the values proposed for maximum permissible doses are such as to involve a risk which is small compared to other hazards of life, nevertheless, in view of the incomplete evidence on which the values are based, coupled with the knowledge that certain radiation effects are irreversible and cumulative, it is strongly recommended that every effort be made to reduce exposure to all types of ionizing radiation to the lowest possible level."

It is beyond the scope of this report to detail the diverse recommendations of the NCRP subcommittes and the adoption or modification of those recommendations by the ICRP. However, in the NCRP report on permissible external dose the concept remained essentially unchanged since the early ideas of tolerance dose and was defined as:

> "...a dose of ionizing radiation that in the light of present knowledge is not expected to cause appreciable bodily injury to any person at any time during his lifetime."

The phrase "appreciable bodily injury" means any bodily injury effect that a person would regard as being objectionable and/or competent medical authorities would regard as being deleterious to health and well-being. Dose, as used in the definition, refers particularly to tissue dose in the irradiated tissue or organ.

The NCRP report defines and discusses critical organs and effects of concern. These were listed as skin, blood forming organs, gonads with respect to fertility and eyes with respect to cataracts.

It was indicated that, when the whole body is irradiated, a rough approximation of the dose in the organ might be made on the basis of an average or effective depth of an organ below the surface of the skin.

Taylor[Ta71] considers the most significant events influencing philisophies in management of radiation protection occurred in the late 1950s. At this time, two studies which reviewed the genetic effects of ionizing radiation were carried out by the Medical Research Council in the United Kingdom and the National Academy of Sciences in the United States[Me56,Na56]. They were apparently conducted with some urgency because of the prospect of thermonuclear testing in the near future. The groups working in the two countries pursued their investigations quite independently but arrived at similar conclusions. The reports were released simultaneously.

The principal conclusion was that the limitation on human radiation exposure should be set by relation to the genetic hazard involved. All radiation exposures were assumed to be cumulative. It was also assumed there was no cellular recovery of any radiation genetic damage and there was a linear relationship between dose and effect down to zero dose. The model was primarily based on the early Drosophila experiments, which demonstrated that a radiation induced mutation was transmitted to successive generations.

There was at this time no clear quantitative assessment of risk to germ cells due to ionizing radiation, but the realization that mutations so produced would be evident in subsequent generations required that a large margin of safety be allowed.

A main recommendation was that no radiation worker should receive more than a total cumulative dose to the reproductive cells of 50 R to age 30 and not more than an additional 50 R up to age 40. In practice this meant limiting occupational exposure of individual radiation workers to 5 Rems per year.

Apparently the NAS study group, before making its recommendation, consulted with the U.S. Atomic Energy Commission and requested the range of practical radiation levels that were reached in normal operations. The AEC reported that it was rare for any person to exceed more than about 1/10 of the permissible occupational exposure allowed at that time. In other words, average individual exposures were around 1.5 Rems per year (permissible exposure level at that time was 15 Rems per year). Also in that year a joint meeting of the ICRP and ICRU resulted in a refinement of the term permissible dose:

> "...the permissible dose for an individual is that dose, accumulated over a long period of time or resulting from a single exposure, which in the light of present knowledge carries a negligible probability of severe somatic or genetic injuries; furthermore, it is such a dose that any effects that ensue more frequently are limited to those of a minor nature that would not be considered unacceptable by the exposed individual and by competent medical authorities. Any severe somatic injuries (e.g. leukemia) which might result from exposure of individuals to the permissible dose would be limited to an exceeding small fraction of the exposed group; effects such as shortening of life span, which might be expected to occur more frequently would be very slight and would likely be hidden by normal biological variations. The permissible doses can therefore be expected to produce effects that could be detectable only by statistical methods applied to large groups."

The recommendation by the National Academy of Sciences that occupational exposure be limited to the order of 5 Rems per year was approved by the ICRP in its 1956 meeting.

By 1958, new experimental evidence concerning the genetic effects of ionizing radiation cast doubt on the concepts expressed a few years earlier. Results of the new work were presented in hearings held by the joint committee on atomic energy on the "environmental effects of producing electric power"(Pa56,Bi56,Co59). Prior to 1958, concepts on genetic damage had been based on work with the fruit fly which indicated that there was no threshold dose or threshold dose rate of radiation for genetic damage.

This concept was challenged by Russell when he showed that mice, given radiation doses spread out in time and delivered at a low dose rate, produced less genetic damage than the same dose given in a short time at a high dose rate(Oa61). This finding has been confirmed by independant investigators(Re66).

The controversy was resolved by consideration of sex differences of animals used in the experiments.

It was judged from this new genetic data that the average genetic risk from exposure of both sexes at low dose rates or low doses is only about 1/6 of what it was estimated to be in 1956. Despite this reevaluation, raising the permissible dose level was not considered.

It is interesting to reflect that while concepts and approaches to radiation protection have changed since 1956, the specified maximum whole body dose of 5 rem/year has remained. Todays 5 rem/year standard was originally developed because of a perceived genetic risk. Concerns about genetic risks came from studies, in the late 1920s, on mutations in fruit flys.

In 1958 ICRP made concerted efforts to reach some uniform approach for determining internal dose and permissible limits for the whole body and various body organs.

Maximum permissible concentrations and body burden values are selected and derived by using mathematical models to estimate the body burden of radionuclides. These MPC values are given for a 40 and 168 hour week. Taylor states regarding MPC values that:

> "...although recognizing that the MPC values were in many instances, based on very incomplete and, in some cases, uncertain data, they nevertheless were felt to embody the latest and best knowledge and constituted the best MPC values available ... when radioactive contaminants are once deposited in the body it is often difficult to make an accurate estimate of the total body burden or its distribution in the body."(Ta71)

Significantly, Taylor highlights a rationale behind occupational exposure hazards in radiation protection. With regard to MPC values he states:

> "...in the light of present knowledge occupational exposure for the working life of an individual at the maximum permissible value as recommended in the report is not expected to entail appreciable risk or damage to the individual or to present a hazard more severe than those commonly accepted in other industries. This is of course the general premise upon which occupational exposure standards are based." (emphasis added)

In 1959 the rate of 0.3 Rem per week was reduced to the average weekly body total dose of 0.1 Rem per week. The purpose of this reduction was to lessen the possible incidence of certain types of somatic damage such as radiation induced leukemia and shortening of life span. The move may have reflected concern that leukemia and other latent effects which were starting to be noted in survivors of the Japanese bombings. ICRP report number 1 noted that:

> "...the direct estimation of the body burden or of the dose to an organ or to the total body was generally difficult and because in most cases measures to decrease the body burdens were rather ineffective and difficult to apply."

Indeed, stating permissible body burdens and organ doses is acceptable, but in realtiy the only practical procedure for general protection of occupational workers was to limit concentration of the various radionuclides in water, food or air(Re59,Re60).

In ICRP publication 2 (1959) the embryonic beginnings of the ALARA principle are discussed in paragraph 45 which reads:

> "...it is emphasized that the maximum permissible doses recommended in this section are maximum values; the Commission recommends that all doses be kept as low as practicable, and that any unnecessary exposure be avoided."

By 1962, ICRP included a discussion of dose rate effects. The commission suggested (on some experimental and theoretical bases which were not discussed in detail) that when either the total dose or the dose rate was very low, any noted effects would be proportional to the total dose and would be independent of the dose rate. This assumption had been implicit in past recommendations on permissible levels. Although unequivocal confirmatory proof is lacking, the assumption is still used as a basis for radiological protection.

In the 1962 report, special attention was given to the exposure of women of reproductive age. For occupational exposure it recommended that when a pregnancy had been diagnosed arrangements should be made to ensure that the exposure of the woman is such that the average dose to her fetus during the remaining period of her pregnancy does not exceed 1 Rem.

By 1966 ICRP had published the evaluation of risks from radiation (ICRP No. 8)(Ev66).

This report marked a significant change in the direction and attention of the ICRP. The now well established delayed appearance of leukemia and other maligancies in the surviving population of Nagasaki and Hiroshima had firmly entrenched the fact that low level exposure resulted in delayed somatic injury. The report also addressed changes in somatic chromosomes of man as well as germ cells.

The task to find some basis for judging the genetic risks to man in some way comparable to somatic risk was confronted in this report. The report outlined dose mutation relationships which might be used for the prediction of such risks. Risk, according to this report, could be defined in terms of orders of risk. For example a fifth order risk implied that the probability of an event such as death or injury would be in the range of 10^{-5} to 10^{-4} or 10 to 100 injuries per million exposed people. The report pointed out that the emphasis which they gave to the limitation of such current assessments, should not be regarded as:

> "...implying that the knowledge of the effects of low levels of radiation is any <u>less</u> precise than the effects of other toxications or environmental factors which cause similarly infrequent effects." (emphasis added)

The use of the phrase "any less precise" implies that the committee believed considerable precision existed in estimates of the toxic effects of other agents. Perhaps a more appropriate phrase would have been "any <u>more</u> precise".

Risk estimates of this kind are made on the basis of data which largely relates the exposures of high doses received during a limited period. Often the data is from animal experimentation. All estimates of effects of low doses and low dose rates are made on the basis of a linear dose effect relationship below the doses at which quantitiative information has been obtained.

Taylor's[Ta71] comment on the 1966 report was:

> "...it was apparent that the report could provide no simple solution to the practical dilema in setting precise criteria for radiation protection."

It is difficult to assess the reasons for the considerable and sudden interest of ICRP in risk assessment. However, it is possible that the proliferation of nuclear power stations and growing public apprehension required clearer perceptions of risk (expressed in numbers). Such perceptions would justify, if necessary, the considerable costs of reducing exposure levels and increasing safety. The attention of the IRCP turned at this time from the establishment of "safe" limits to the evaluation of risk. This change in approach marked a significant stage in the philosophy underlying radiation exposure standards.

In summary, by 1962, the historical development of radiation protection had undergone three major stages:

1. Standards based on the absence of effects such as skin erythema.
2. Standards based on a perceived genetic risk.
3. Standards based on the concept of acceptable risk.

By 1965, a further development stage was completed by the first direct expression of the ALARA principle which was detailed in ICRP 9, paragraph 52.

> "As any exposure may involve some degree of risk, the Commission recommends that any unnecessary exposure be avoided, and that all doses be kept as low as readily achievable, economic and social considerations being taken into account." (emphasis added)

In 1975 the wording had changed. ICRP Publication 22, paragraph 20, noted:

> "...to provide for operational control of specific procedures, both individually and in combination, so that the resultant doses are as low as reasonably achievable, economic and social considerations being taken into account." (emphasis added)

and by 1977 ICRP 26 states in paragraph 12:

> "...all exposures shall be kept as low as reasonably achievable economic and social factors being taken into account." (emphasis added)

The various word and phrase changes over the years seem to reflect a variety of slightly differing perceptions and interpretations of the ALARA principle.

From 1977 on, epidemiological data from many concerted studies on late consequences of ionizing radiation became available and it became possible to apply industrial type risk figures to the consequences of ionizing radiation.

18.0 PRESENT SYSTEM OF STANDARDS FOR IONIZING RADIATION

Many of the recommendations of ICRP Publication 2 concerning internal radiation exposure from the intake of radionuclides were adopted by Western countries and certain interpretations of the recommendations are still in use today. It was recognized though, that situations existed where a radiation worker could be exposed to a uniform radiation field from a source external to the body and that this same worker could also have intakes of radionuclides via inhalation, ingestion or skin absorption. In the assessment of overall dose in such a situation, the external exposures were treated separately and compared with the 5 rem/year limit. However, the internal exposures were treated according to the critical organ concept described in ICRP Publication 2 and total dose equivalent was not to exceed 5 rem/yr.

The critical organ concept has drawbacks. Its use in deriving secondary limits, such as the Maximum Permissible Concentration (MPC), ignores the exposure to other organs, which must inevitably occur during translocation from the entry point (lung, skin or stomach). Thus, although a radionuclide would concentrate selectively in high concentrations in a particular organ, other organs may have low concentrations. Considerations of organ concentrations pre-occupied the ICRP in the early 1970s as they sought to unify the internal and external exposures under one concept. One can intuitively sense that the risk from exposure to ionizing radiation must be the same for internal and external doses. Put another way, if a radiation worker receives external and internal doses of equal magnitude, then the risk should be additive, taking into account both types of exposures.

ICRP published their major revision in radiation protection philosophy in 1977 as Publication 26. The annual whole body dose limit of 5 rem (50 mSv) was not lowered. However, there is an extensive discussion of radiation effects in terms of risk and a method for unifying internal and external exposures is provided in this publication. Two types of effects are defined in Publication 26: stochastic and non-stochastic . The word stochastic is employed in mathematics (statistics) and relates to probability. Stochastic effects are those for which the probability of occurrence, not the severity, is a function of dose with no threshold (e.g., carcinogenesis, hereditary effects, etc.). Non-stochastic effects are those for which the

severity of effects are a function of dose, with a possible threshold (e.g., cataracts, fertility impairment etc.). ICRP Publication 26 defines the aim of radiation protection as follows:

> "...to prevent detrimental non-stochastic effects and to limit the probability of stochastic effects to levels deemed to be acceptable ... and to assure that practices involving radiation exposure are justified."

The three key principles of dose limitation recommended in ICRP Publication 26 are:

1. No practice shall be adopted unless its introduction produces a net positive benefit.
2. Exposures shall be kept as low as reasonably achievable, economic and social factors being taken into account (ALARA).
3. The dose equivalent to individuals shall not exceed the limits recommended for appropriate circumstances by the Commission.

In order to prevent injuries on the non-stochastic level, a limit of 50 rem per annum is imposed as a maximum permitted dose for any part of the body. The notable exception is the lens of the eye for which a dose of 30 rem (300 mSv)/year was recommended but later changed to 15 rem (150 mSv)/year. The limit for the lens was reduced to 150 mSv/year after the ICRP meeting in Brighton, March 1980. Stochastic effects can be kept within acceptable levels, according to Publication 26, by keeping justifiable exposures below the whole body dose limit of 5 rem (50 mSv)/year.

Justifiable exposures now include both internal and external components and their sum or combined value must be held within the 5 rem (50 mSv)/year whole body limit. The problems of defining a whole body dose based on internal exposures is tackled in Publication 26 by assigning a weighting factor to various organs and tissues which reflect all the known factors of radiosensitivity. The weighting factor is then used to arrive at the contributor to effective dose equivalent.

ORGAN TISSUE	STOCHASTIC EFFECT	RISK	WT
Gonads	Genetic effect	$4 \times 10^{-3} Sv^{-1}$	0.25
Red Bone Marrow	Leukaemogenesis	$2 \times 10^{-3} Sv^{-1}$	0.12
Bone Surfaces	Osteogenesis	$5 \times 10^{-4} Sv^{-1}$	0.03
Lung	Lung cancer	$2 \times 10^{-3} Sv^{-1}$	0.12
Thyroid	Thyroid cancer	$5 \times 10^{-4} Sv^{-1}$	0.03
Breast	Breast cancer	$2.5 \times 10^{-3} Sv^{-1}$	0.15
Other Tissues	Cancer	$5 \times 10^{-3} Sv^{-1}$	0.30
			1.0
TOTAL RISK OF STOCHASTIC EFFECTS		$1.65 \times 10^{-2} Sv^{-1}$	

The risk factors are based on epidemiological data of uniform whole body exposures from external sources. The weighting factors W_T are based on relative susceptibility of the organs to stochastic effects. Therefore, in the case of non-uniform exposures such as would occur from intakes of radionuclides in the body, a mechanism is established whereby it is possible, using dosimetric models and weighting factors to estimate a dose value which gives the same total stochastic effect as a uniform whole body exposure from external radiation. A new term called the "effective dose equivalent" was introduced to express this procedure of combining organ doses and weighting factors. (The concept first appeared in ICRP 26, but the name came later.) Because the effective half-life of radionuclides in a given organ may range from a few hours to several years the integration period is roughly equal to the occupational work life (18-65 years). This consideration led to another term called the "committed effective dose equivalent". The term effective dose equivalent refers to the internal and external partial body doses (from an external radiation field) received from a given year's intake in that particular year. The term committed effective dose equivalent refers to the dose equivalent that will accumulate during the 50 years following the intake of a radioisotope. It is clear that where the effective half-lives are short (hours to a few days) the effective dose equivalent and the committed effective dose equivalent become identical. However, for effective half-lives of greater than 100 days, the committed effective dose equivalent will be greater in magnitude than the effective dose equivalent.

Using the conservative approach, Publication 26 recommends that the committed dose equivalent (later called effective dose equivalent) from a year's operational practice be used in

summation with the external whole body dose and that this sum be kept below the 5 rem (50 mSv) limit. The implications of this recommendation in terms of acceptable measurement methods and additional engineering controls that may be required in facilities which handle radionuclides with large effective half-lives, have caused a significant amount of debate in the health physics profession over the last 3-5 years.

With respect to the ALARA principle advocated in Publication 26, ICRP recommends the use of cost-benefit analysis to determine the level of dose reduction below the applicable standard. ICRP suggests that a balance be struck between the incremental costs of reducing radiation exposures and the reduction in detriment (or harm) to the exposed population. Having made such a recommendation ICRP recognized that assessment of detriment or harm is a subjective exercise and Sir E.E. Pochin was commissioned to address this issue. Pochin's work, titled "Problems Involved in Developing an Index of Harm", was adopted by the ICRP and recorded as Publication 27. In Publication 27 an attempt is made to relate risks of fatalities in other industries, through accidents and occupational diseases, to the risks due to fatal malignant disease caused by radiation. It is instructive to quote paragraph 74 of Publication 27:

> "Continuous annual exposure of every worker at the Commission's limit of 5 rems per year would yield an index of 0.4 + 7.5 + 2.0 + 1.6=11.5, equivalent to an occupation with a fatal accident rate of 340 x $10^{-6}y^{-1}$, comparable with that in construction work or coal mining."

While admitting certain limitations about the type of approach and data set used, Publication 27 indicated that some "index of harm" is necessary to compare the safety of occupations in nuclear facilities with that of other existing occupations. (There appears to be an implicit appeal for understanding of the radiation protection standards, in the sense that 'society' should not expect one level of safety standards for radiation protection and a different level for other types of hazards.)

Pochin's ideas have since been further justified and developed (though not fundamentally changed) in ICRP 45 (1985).

In ICRP Publication 2 (1959) methods were given to calculate the secondary or derived limits called MPCs, for concentrations of various radionuclides in air and water. The MPCs were based

on the concept that if a person was exposed under chronic conditions to concentrations at these limits, then at the end of a 50 year period the organ would attain a radionuclide burden corresponding to the maximum permissible dose (for radionuclides with long half lives). These MPCs were the first set of secondary internal radiation 'standards' and they were adopted by regulatory agencies (e.g., U.S. 10 CFR Part 20). Between 1959 and 1977, there was a significant growth in knowledge relating to health physics. In particular, better metabolic models were derived for alkaline earths (ICRP 20, 1973), the respiratory system(Tg76), the gastrointestinal tract(Eve66) and the skeleton(Sp68). Therefore, the MPC values needed review. Closely following the release of Publication 26, ICRP published in 1979 a report titled "Limits for Intakes of Radionuclides by Workers" (ICRP Publication 30).

Using the dose limit constraints specified in Publication 26 in conjunction with improved metabolic models and specific metabolic data for some radionuclides, ICRP has presented a scheme in Publication 30 (1979) to limit the effects by estimating the intake quantities of radionuclides which give a committee effective dose equivalent not exceeding 5 rem/yr (50 mSv/yr). In addition, for any single organ or tissue the annual dose equivalent should not exceed 50 rem (500 mSv) to remain below the threshold for non-stochastic effects. This applies specifically to radionuclides that have affinity for organs with low W_T values (thyroid, bone surfaces, or organs under the remainder category). These intakes are called the "Annual Limit of Intake" (ALI) and are given in units of becquerels (Bq). Values of ALI are given in Publication 30 for the oral and inhalation route of entry. Derived Air Concentrations (DAC) are also given for the cases of inhalation ALIs by assuming a breathing rate for standard reference man and an occupational work year of 2,000 hours. ICRP cautions that:

> "...the limit for inhalation is the appropriate ALI, and that the values of DAC (Bq/m^3) for a 40 hour work week are given only for convenience and should always be used with caution."

This admonition is given because the ICRP was concerned about the misuse and misinterpretation of its previous derived limits (Maximum Permissible Concentration values), which some interpreted as limits that should never be exceeded. According to ICRP the MPC concept is no longer valid. ICRP Publication 30 supersedes ICRP Publication 2 and this is clearly stated in the opening page.

In Publication 32 titled "Limits for Inhalation of Radon Daughters by Workers" (1981), ICRP extended the concept of ALI to radon daughter exposures. The recommended ALI value is based on the work of Jacob and Eisfeld[Ja80] and James et al[Jag80]. One ALI for radon daughters is estimated to be equal to 0.02 Joules. From this relationship and the definitions of working level (WL) and working level month (WLM) it can be deduced that 4.7 WLM results in an effective dose equivalent of 5 rems (50 mSv) per annum.

To a large extent, the validity of the ALI values in Publication 30 and 32 depend on the assumptions incorporated into the dosimetric models and the calculational techniques. Despite being subjected to several critiques since publication, the concept of ALI is a significant improvement in understanding, (over Publication 2), of doses imparted by radionuclides taken into the body. ALI values in Publication 30 are given for aerosols of particle size 1 micron (AMAD) and a method for modifying these values for other particle sizes is also given.

19.0 COMPARISON OF THE RATIONALES USED IN STANDARD SETTING FOR CHEMICALS AND IONIZING RADIATION

The comparison of the rationales requires more than a simple delineation of the factors involved in establishing TLVs for the ten chemicals in this report with the factors involved in establishing comparable limits for radiation exposure. A direct comparison of this type would be overly simplistic since it does not take into account the sometimes substantially different purposes, objectives, concepts and principles used in workplace chemical protection and in radiation protection. Any comparison must take into account the differences in these features.

The publication ICRP 26 is used as the basis for the comparison. There is no equivalent to ICRP 26 for chemical exposures in the workplace and comparison with the existing situation in occupational health toxicology is based on the knowledge and experience of the authors of this report.

19.1 Origins of the Standard Setting Organizations

ACGIH has been responsible for establishing the philosophy behind and recommended TLVs for limiting workplace exposure to hazardous chemicals throughout the western world, but it was never conceived as an international body. Originally, ACGIH was seen purely as a U.S. organization developing guidelines only for exposures in the United States.

However, over the years ACGIH suggested limits have been adopted internationally. This adoption of American guidelines was probably assisted by the spread and investment of American industry abroad and by the reluctance of other countries to devote resources to establishing their own unique national principles or standards. ACGIH now has a few members from other countries to give it some international scope.

ICRP membership on the other hand, is more truely international and clearly attempts to establish international uniformity in the philosophy, concepts and recommendations applied to radiological protection. Individual countries obviously have sovereignty over the exact standards enforced, but the philosophy and concepts used are largely those developed by ICRP.

19.2 Objectives of the Standards

19.2.1 The Protected Population

Paragraph 6 of ICRP 26 states that:

> "...radiation protection is concerned with the protection of individuals, their progeny and mankind as a whole."

No such broad objective is stated for workplace chemical protection. The standards are intended only for those employed in the manufacture or use of chemicals.

19.2.2 The Focus for Protection

ICRP 26 states that:

> "...the detrimental effects against which protection is required are known as somatic and hereditary."

While these terms are known in occupational toxicology, the focus of protective policies in the workplace is almost entirely aimed at somatic effects. While possible effects on heredity are often a concern, they receive little attention in the development of threshold limit values. This is largely because, for most chemicals, there are no studies on reproductive function or capacity. In contrast, the need to protect against hereditary effects of radiation was identified early in the history of health physics. ICRP publications in 1958 and 1959 placed great importance on exposure levels that would prevent genetic calamity even though, by this time, the risk of such calamity was suspected only and judged to be small.

ICRP 26, paragraph 7 defines "stochastic" and "non-stochastic". These terms are unknown in occupational health toxicology. Stochastic effects include those produced as a function of dose without threshold. Examples are hereditary effects and carcinogenesis. Non-stochastic effects are those in which the severity of effect varies with dose and in which a threshold may occur.

ICRP 26, paragraph 96 discusses dose equivalent limits for workers, and states that:

> "...radiation exposure at levels imposed by adherence to recommended dose equivalent limits, is expected to cause very few injuries or illness in exposed workers other than any malignant diseases which may be induced." (emphasis added)

Paragraph 97 states:

> "...the non-fatal effects of irradiation are much less frequent than the non-fatal effects encountered in other safe occupations." (emphasis added)

Finally, paragraph 103, states:

> "...the Commission's recommendations are intended to prevent non-stochastic effects and to limit the occurrence of stochastic effects to an acceptable level."

These statements, taken together, imply that the emphasis of radiological protection is to limit stochastic effects and to eliminate non-stochastic ones. These points underline a fundamental difference in the emphasis of the objectives of radiation protection as compared to those for protection against workplace chemicals. Protection in occupational health is primarily the prevention of non-stochastic effects. Non-stochastic effects occur far more frequently in workplace chemical exposures than in workplace ionizing radiation exposures.

ACGIH, the standard setting organization in occupational health, considers that chemical carcinogens have a threshold despite the absence of any evidence for or against this assumption. Relatively few chemicals are considered by ACGIH as carcinogens. ICRP considers carcinogenesis:

> "...the chief somatic risk of irradation at low doses and therefore the main problem in radiation protection."

In occupational toxicology, the focus for most chemicals is on the acute effects occurring at high doses over short periods of time.

Even for those chemicals which cause chronic toxicity, such as the ten reviewed in this report, the standards may be set on

the basis of preventing short-term effects rather than chronic disease. For example, the TLV for hydrogen fluoride is set to prevent irritation, not fluorosis. The TLV for nitroglycerine is set to prevent headache, after inurement, rather than chronic heart or nerve system disease.

For three of the chemicals in this report which had safety factors, namely mercury, n-hexane and cadmium, the emphasis of ACGIH parallels that of ICRP. For these three chemicals ACGIH essentially follows the objective stated in ICRP 26, paragraph 10 regarding the prevention of non-stochastic effects where:

> "dose equivalent limits [are set at] sufficiently low values so that no threshold dose would be reached even though following the exposure for a whole life time or for the total period of a working life."

Only for one chemical, namely vinyl chloride (as designated by the Ontario Ministry of Labour), does the standard setting rationale parallel that used by ICRP for stochastic effects. This rationale aims at limiting stochastic effects to an acceptable level through a risk assessment analysis. Even here there are differences since the malignancy which may appear due to vinyl chloride (angiosarcoma) is <u>characteristic</u> of vinyl chloride exposure.

However, similarities end here for, in radiological protection, stochastic effects are limited by keeping all justifiable exposures:

> "...as low as is reasonably achievable, economic and social factors being taken into account, <u>subject always</u> to the boundary condition that the appropriate dose equivalent limits shall not be exceeded." (emphasis added)

With the exception of toluene diisocyanate and silica in the Ontario regulations there is no ALARA principal invoked either implicitly or explicitly for any of the ten chemicals discussed in this report. Even in the case of TDI and silica under the Ontario regulations the ALARA principal seems to be used more as a gesture to accomodate industries with old technolgy than to achieve 'safe' working levels.

A further interesting feature of the ICRP ALARA statement is that economic and social factors <u>defer</u> to the dose equivalent limit. This is not so in occupational health where economic factors are taken into consideration during the standard setting process.

19.3 Basic Concepts

In ICRP 26, paragraphs 15 and 16, the Commission introduces the basic concept of detriment in order to identify and where possible quantify all deleterious effects. No such equivalent concept exists in occupational health toxicology and the mathamatical expression of it would be considered highly speculative and impractical.

ICRP 26, paragraph 17 discusses and defines dose equivalent which was created to correlate better than dose with the delayed stochastic or the non-stochastic effects. It is here that a further fundamental difference occurs between the underlying concept of radiation protection and that for protection against workplace chemicals. In health physics dose (expressed as effective dose equivalent) forms the basis for providing worker protection. Dose seems to be well defined for external but not for internal radiation exposures. However, protection against chemicals in the workplace is not achieved by specifying organ or whole body chemical doses. Rather it is achieved by specifying permissible airborne exposures. As will be discussed later, in occupational health the terms exposure and dose have become confused and are often mistakenly equated. While the two are not generally confused in health physics, it is interesting to note that radiation doses to the whole body or other organs cannot be measured directly. Dose can only be estimated indirectly in health physics by measuring exposure. The idea of using 'permissible doses' rather than exposures has never been considered very practical in occupational toxicology. The total dose of a chemical received by an organ or a whole person cannot be accurately measured. Frequently, blood, urine or tissue levels of a chemical show little or no relation to the degree of exposure and at best are only tentative estimates of dose. Further, the detailed metabolism of most compounds is unknown and in many instances it is uncertain if the workplace chemical or one of its metabolites is responsible for a given toxic effect.

Until quite recently the unknowns and variables of the body's chemical metabolites were considered so great that there was little practical purpose in dwelling on body or organ doses. Recently six chemicals were given permissible dose level values (called Biological Exposure Indices (BEIs)) because in the case of these few it was judged that sufficient knowledge existed about their metabolism and their dose relation to health effects. It is facinating to note that all the uncertainties concerning chemical metabolism have not detered health physics

from developing an abundance of dose limit guidelines which are set out in ICRP 30. All of these dose limits are derived by the use of mathematical models which are based on a review of often limited knowledge about the metabolism of chemicals. The inescapable conclusion from the dichotomy of the two approaches is that health physicists have much more faith in data extrapolation from limited knowledge bases than do their counterparts in occupational toxicology.

ICRP has further refined the concept of dose by developing dose-equivalent commitment and committed dose equivalent for instances of extended exposure (for retained radionuclides only). No equivalent quantities exist in occupational toxicology though the importance of extended exposure time in the development of chronic disease is well recognized.

19.4 Dose Response Relation

With respect to non-stochastic effects, there is litte difference in the concepts of dose and response between radiation and chemical protective fields. In both toxicology and radiation knowledge of dose response relation is too limited to enable confident prediction of shapes of curves at low doses or low dose rates.

On the question of dose-rate and total dose in the region of low doses NCRP report 64 "Influence of dose and its distribution in time and on dose response relationships for low-level radiations", discusses this problem. Animal experiments indicate the slope of the dose response curve (for several end points) increases with increasing dose-rate in the region of intermediate dose. In the low dose region the curves for low dose-rates merge. Most of the human epidemiology is at intermediate and high dose range. NCRP base their judgement on animal data, with regard to human application.

Paragraph 30 of ICRP 26 discusses the use of linear extrapolation from the frequency of effects observed at high doses. None of the chemical TLVs discussed in this report were derived by extrapolation from high doses in order to derive an estimate of the risk at low doses. Where data at low doses was missing, levels were selected arbritarily and could be categorized as judgemental values.

For stochastic effects ICRP has a "without threshold" assumption. In contrast, ACGIH considers that carcinogens have thresholds. A very fundamental concept in health physics is that at low total doses or low dose rates ionizing radiation causes effects that result from cumulative doses. No comparable tenet is held for chemicals and it is generally assumed that homeostatic mechanisms of biological repair prevent or retard cumulative effects.

19.5 Tissues at Risk

ICRP 26 discusses various biological tissues considered to be at risk from ionizing radiation exposure. While toxicology studies often refer to target organs and critical doses within target organs, the critical dose concept is rarely used as a determinant of an occupational exposure level. Only in one of the ten chemicals discussed, namely cadmium, were there indications that this kind of approach might form part of the standard setting process used by the Ontario Ministry of Labour.

The problem with the critical dose approach is that it requires extrapolation from animal data to humans. Determination of a critical dose that causes irreversible damage to the human kidney is exceptionally difficult, if not technically and morally impossible. Again, while the problems of derivations also apply for ionizing radiation at high levels it has not deterred such derivations for use in health physics.

19.6 The System of Dose Limitation (Cost/Benefit Analysis)

ICRP 26 discusses questions of cost/benefit analysis. It is evident from the discussions in paragraph 68 to 76 that the procedures used for such analyses in radiation protection are essentially similar to those found in occupational health. No formula exists in occupational toxicology to derive a net benefit as shown in paragraphs 73 and 74. The mathematical derivations shown in these sections seem rather theoretical and impractical, to say the least.

Perhaps the best summation of the situation in both radiation protection and in occupational health toxicology is the statement in paragraph 71:

> "...it may thus be necessary to make subjective value judgements in order to compare the relative importance of the costs imposed on human health by radiation (or chemical) exposure with other economic and social factors." (words in parentheses added)

There is no question that for some of the ten chemicals discussed, economic considerations played an influential role in setting the exposure standards. Indeed, industry seems to be heavily involved with ACGIH in the standard setting process and economic considerations seem largely to focus on weighing the extent of the risk that exposure involves with the cost to industry of introducing control procedures which would reduce the exposure level. In discussing the role of industry in this process, Stokinger wrote:

> "...plant industrial physicians and engineers are making observations on the workers and their workplace environment. Some TLVs so derived have been based on a decade or two of industrial experience ... clearly, such procedures can yeild indisputable data on which realistic TLVs can be derived, unsurrounded by that uncertainty and doubt which requires the incorporation of large safety factors, leading to wasteful over-engineering of plant processes."(St70)

It is interesting that Stokinger, and presumably the industry whose concerns he is voicing, have not considered that over-engineering might be beneficial rather than wasteful relative to the company's economic efficiency. However, the clear influence of the economic approach is brought home when Stokinger continues by claiming that:

> "...TLVs provide safety without over protecting the worker or over-engineering the plant processes, practices which private enterprise can afford only at the expense of the consumer public which pays the increased cost of their product."

As chairman of the ACGIH committee, he indicated the cost benefit considerations which go into the decision making process of selecting a standard by stating:

> "...it is not enough merely to define the dose that will produce a borderline response. The next important step is to determine whether the response at the defined dosage has any overall physiologic significance to the industrial worker, who is on the job day-after-day, and may become inured through homeostatic mechanisms ... Not to make the determination of physiologic significance can result in undue alarm for health and safety of the worker and more important, can result in costly over-engineering costs that are ultimately passed on to you and me the consumer." (emphasis added)

In standard setting systems for chemical exposures, it is apparent that the concern for workers health is tempered by a perceived economic need to avoid costly over-engineering.

In contrast, ICRP does not directly consider the costs, management or implementation of its recommendations at the industrial level. These considerations are left to the agencies and authorities responsible for radiation protection in each jurisdiction. ICRP makes its recommendations seemingly on the basis of health criteria and theoretical concepts. The practical application of these recommendations does not appear to be a major consideration in the ICRP standard setting process. In this respect, ICRP seems to parallel NIOSH rather than ACGIH.

19.7 Choosing the Numbers for Standards

For workplace chemical exposure standards, Stokinger(St70, St69) noted with respect to the 414 TLVs set in 1968 that:

> "...38 per cent made use of the responses of the industrial worker, and that chronic animal inhalation studies were employed about half as frequently (20 per cent). It is interesting to note that the development of TLVs by analogy accounted for about one-quarter of the procedures used. Human volunteer studies were responsible for about 1 in 10 of the limits, and the remaining animal procedures (other than chronic inhalation) accounted about 1 in 14 limits."

The statement implies that only scientific data are considered in establishing TLVs. There is no indication of any compromises due to economic considerations, compromises that were apparent in several of the ten chemicals reviewed in this report.

In order to protect against chemically induced disease conditions, ACGIH attempts where possible to find human exposure data that will indicate a threshold level below which the adverse health effects will not occur, or will not be noticed in the short-term.

As demonstrated in some of the ten chemicals discussed in this report, the search for a threshold extends even to diseases caused by low level, long-term exposure. In some instances, relatively low dose levels are known to produce detrimental effects if exposure is continued over prolonged periods.

Perhaps the best way to visualize the TLV standard setting process is to refer to the impairment-disability curve, developed by Hatch(Ha62) (Figure 2). According to this curve impairment increases as environmental stress increases. The TLVs for mercury, n-hexane, cadmium and vinyl chloride probably fall near point A on the curve. TLVs for cobalt, hydrogen fluoride, and TDI seem to fall somewhere between point A and permanent disability while silica, carbon disulfide and nitroglycerine may be anywhere from point A to fatal.

Professional judgements are made to balance the knowledge concerning the homeostatic range with the perceived costs to industry. In some instances, the standard chosen may be in the B to 'repair' range or even the permanent disability area. Only those TLVs with safety factors probably fall close to point A.

On this subject it is worthwhile remarking that there is no set method for determining the magnitude of a safety factor. Stokinger noted in 1972 that the choice of safety factors:

> "...depends on the seriousness of the response"

and that safety factors are:

> "...all judgemental values derived from the long experience of the TLV committee members."(St72)

In some instances such as TDI, NG, carbon disulfide and hydrogen fluoride it is evident that some workers would be affected. The idea that health effects would occur in some people gained acceptance early in the history of standard setting for chemicals. In 1948 Elkins(El48) wrote:

> "...if the illness is rather minor and transient the (standard) can be chosen at a level which does affect a minority of workers, but should be below the value where the average individual suffers."

The idea that 'minor' health effects should be ignored for the purposes of standard setting is quite evident for the four chemicals TDI, NG, carbon disulfide and hydrofluoric acid.

Even in the small sample of ten chemicals reviewed in this report, the disparity surrounding the application and magnitude of safety factors is evident. For TDI, hydrofluoric acid, cobalt, NG/EGDN, silica and vinyl chloride, a no-effect level has not been determined. Stokinger observed that:

> "...it is not uncommon to find that the 'no-effect' level is one-fifth, or one-tenth or less that at which minimal effects occur."(St72).

A statement entirely incongruous with the disparate and arbitary values applied in practice.

In summation, the process of deriving a threshold limit value is highly variable. Almost every chemical is considered on an independent basis and the weight which is given to health effects, economic and technical feasibility, safety factors and risk extrapolation varies from chemical to chemical. The result is a somewhat ill-defined process showing a heavy dependence upon the professional judgement of members of the ACGIH committee and little adherence to any standardized procedures or principles.

Choosing the figures for radiological protection seems little better from the scientific viewpoint in that the values selected are also judgemental. Typical of the process is that reported by Robley D. Evans in his paper "Inception of Standards for Internal Emitters, Radon and Radium..."(Ev81). After reviewing several human cases and animal studies he and his co-workers appreciated that the available data was inadequate for the determination of absolute values for permissible doses. Evans noted:

> "...we were obliged to make an 'informed judgement' decision, I suggested that we should set the 'tolerance level' for residual radium burden in radium-dial painters at such a level that we would feel perfectly comfortable if our own wife or daughter were the subject."

Such 'informed judgement' decision seems to be the basis of other primary standards used in health physics and to some degree parallels similar judgemental processes in occupational health.

However, standards chosen and derived in health physics do have considerable edge over many of those developed for occupational health. The edge is that the entire permissible dose structure of health physics is based on the inability to observe any deleterious or other effect(Ta81). In addition, large safety margins seem to be incorporated into the judgement process. This is not so for many chemicals and is certainly not the case for four of the ten discussed in this report (hydrogen fluoride, carbon disulfide, NG and TDI).

While the science underlying the choice of exposure figures leaves much to be desired in both health physics and occupational health, it is undeniable that the determining factors used in health physics (namely lack of observed effect and large safety margins) are clearly superior to those used in occupational health.

20.0 THE SCIENTIFIC VALIDITY OF THE PRINCIPAL CONCEPTS USED FOR ESTABLISHING PERMISSIBLE EXPOSURE LIMITS FOR WORKPLACE CHEMICALS AND IONIZING RADIATION

As noted in the historical section of this report, exposure limits for workplace chemicals were initially expressed as Maximum Allowable Concentrations or Ceiling levels below which all values must fluctuate. In 1953, the ACGIH added a preamble to its TLV booklet indicating, without further explanation, that TLVs were not MACS but time-weighted averages. This change, although quite radical and scientifically unjustified, became widely accepted in the western world. Surprisingly, there is no literature documenting the reasons for the shift to a TWA concept. However, it could be speculated that the change was made to accomodate industry's concerns about always maintaining airborne chemical levels below a specified maximum concentration. Industry undoubtedly favours a system which allows for some excursions above the permissible level during certain stages of a manufacturing processes. In addition, the system accomodates occasional engineering malfunctions. It is perhaps also worthwhile reflecting that standards based on TWA are much more difficult to enforce than those based on the MAC concept.

Until recently, the scientific validity of time-weighted average remained unquestioned. Then, in 1985, Atherley published a critical review of TWA and its key elements(At85). He noted that time-weighted average has become adopted as an index of exposure and dose, and has consequently confounded many occupational health efforts in research, practice and legislation. Except in early health physics literature where Roentgens are often cited both as units of exposure and dose such confusion does not appear to have occurred in the field of radiological protection.

In his review of TWA Atherley indicates that true dose differs from exposure because of internal metabolism and distribution within the organism. Other factors also intervene. These concepts are considered and developed in radiological protection by the use of the dose equivalent H which contains radiation quality, Q, and modifying factors N. D is the physical dose measured in energy per unit mass which creates ion pairs.

$$H = DQN$$

There is no parallel to dose equivalent in toxicology. If an equivalent concept of dose existed, it would probably not require the equivalent of a quality factor, but almost certainly would need a modifying factor. The contribution of the factors comprising "N" in toxicology as in radiation protection cannot be numerically assessed due to lack of experimental evidence. The development of dose equivalent as a toxicological parameter would therefore be unlikely.

The key element of TWA is the product of concentration x time (CT). Both epidemiologists and toxicologists have become accustomed to relying on CT as as expression of dose-response even though it does not constitute a true dose-response relation.

In 1952, Adams et al(Ad52) specified that two conditions were necessary in order to verify TWA. The two conditions involved C and T.

1. The numerical values of CT ... are directly proportional to the severity of toxic effect for all possible values of CT (CT = K).
2. The toxic effect or value of any one component of a days exposure C_aT_a is the same regardless of its chronological relationship to other components C_bT_b etc.

Adams et al pointed out that:

> "... actually it is known that CT does not correctly portray the toxicity value of exposures, although the numerical results may be nearly constant in some instances over limited ranges (condition A). There appears to be no information whatever bearing upon the second condition (condition B). Accordingly, it must be concluded that there is no scientific basis for the use of time-weighted average to integrate varying exposures."

Atherley traces the origin of CT = K back to the German scientist Haber who in 1924 wrote:

> "... a simple and sufficiently practical gauge of toxicity is obtained, if for each toxic gas, we specify the mass C in milligrams present in each cubic metre of breathing air and multiply it by the time T in minutes that this air must be breathed by the experimental animals in order to produce mortal harm. The smaller this product C x T is the more toxic is the war gas." (translation)

In further discussions Haber went on to explain that CT = K has limitations as an expression of toxicity. Further, his expression is a rule for exposure rather than for dose.

In health physics there is no corresponding equation implying that CT produces a constant biologically harmful effect. Maximum permissible concentration in air (MPCa) when expressed as MPCa hours is comparable to C x T and therefore to time-weighted average. However, there is no implication in radiation protection that MPCa x hours produces a constant adverse biological effect.

In his discussion, Atherley concurs with Adams and concludes there is no scientific validation for the use of TWA to integrate exposures and there is even less justification for using it as an index of dose.

Stokinger, who was a member of the TLV committee from 1951 to 1962 and served as its chairman from 1962 to 1977, took great exception to Atherley's criticisms of TWA. In a letter to the editor he pointed out that TLVs are only in part based on time-weighted averages and that all those TLVs which are not based on human data incorporate safety factors to allow for the extrapolation from animal to man(St86). Stokinger's statement is not borne out by the rationale for cobalt reviewed in this report. Stokinger's scientific arguments for the justification of TWA are weak. Rather than tackle the question of the validity of TWA, he replied that:

> "...the proof of the pudding is in the eating and the proof has been clearly evident over the past 40 years ... I cannot recall a single serious hazard to health having occurred, provided exposures were kept within the TLV guidelines."

Stokinger's objections ring somewhat hollow. His argument takes the stance that scientific validity of the basic principles do not matter since over the last forty years TLVs have worked. This confidence in the existing system has in large degree, obscured earlier concerns about the scientific foundations of TLVs. In 1943, Sterner wrote that the permissible exposure limits of the time were:

> "...based on a considerable amount of careful clinical evidence, but many are very tentative in character, and are meant as nothing more than the best estimate as to a safe level."(St43)

Twelve years later, after a meeting which revised some TLVs, he was still concerned about the scientific validity of the limits and wrote that:

> "...even though stricter standards were described which would satisfy a discriminating jury of scientists, the available data for establishing threshold limits for all but a very few substances would fail to satisfy such limits. The real use for threshold limits, as a guide for industry in the control of exposures and as a measure for action by governmental agents, demands a continuing improvement in the quality and quantity of the methods by which truely valid criteria may be achieved." (emphasis added)(St56)

There is no doubt that the absence of any firm scientific foundation for exposure limit levels causes disquiet amongst those occupational health professionals who recognize the limitations of the figures that they apply and use daily in the workplace. The attempts to correlate exposure with dose and toxicological effect continue. Today's occupational health efforts show a growing emphasis on the development of medical procedures which assess the levels of chemicals in the body and their impact in terms of disease.

Schrecker(Sc86) has identified two underlying purposes of the current emphasis on medical measurements of the worker:

1. Growing attention to physiological or behavioural changes as an indication of hazards from exposure.
2. The identification of individuals or groups who may be more vulnerable than others to the effects of a particular chemical (so-called hypersusceptibles).

The first of these purposes is usually achieved through employment pre-screening tests and medical monitoring at intervals throughout employment. It is interesting that medical monitoring procedures are often justified by stating that they serve as a final check on the effectiveness of engineering controls. It is never hinted that medical monitoring might be necessary because of the very tentative nature of the exposure standards and the uncertainies of the science on which they are founded.

Medical monitoring is also justified on the basis that it promotes worker health by the prevention of industrial disease. Rarely is it pointed out that monitoring does not

prevent disease and at best, can only detect it at an early stage. This is small comfort for those who are at risk from developing long-term chronic and progressive diseases such as silicosis or inoperative tumour.

To some degree, medical testing of workers represents an on-going investigation of the dose-response relationship for chemical exposures to humans; a continued search for scientific validity.

A report on the subject in 1950(Ni50) observed that:

> "...if there exists sufficient knowledge of the behaviour of a chemical in the body, the estimation of one of its metabolites may yield a better approximation of the degree of a workman's total daily exposure than can a time-weighted average exposure. Physiologic tests, when sufficiently precise, may supplement hygienic standards of exposure and in doing so avoid present uncertainies about the average man by determining the degree of response of each exposed person."

Such an approach has attraction as it involves reducing uncertainies associated with biological variability, as well as overcoming the uncertainies of the time-weighted average concept. Further, it eliminates the difficulties and 'trans-science' that is associated with extrapolating data from animal studies to human responses.

The ethics of the medical monitoring approach is currently the centre of much heated debate in the occupational health medical community.

The second purpose Schrecker claims for medical monitoring is aimed at the detection of hypersusceptibles. The underlying reckoning or theory here is that certain occupational diseases could be eliminated by prescreening tests that would preclude the entry of susceptible workers into trades where they may succumb to an occupational disease. This approach was voiced even prior to the 1940's when one author discussing 'potters lung' wrote: -

> "...while I am sure that our standards of industrial hygiene are shamefully low, it is important to realize that there is a side of the question which so far has been completely ignored. The majority of potters do not die of bronchitis. It is quite possible that if we really understood the causation of this disease, we should find out that only a fraction of potters are of the constitution which renders them liable to it. If so, we could eliminate potters bronchitis by regulating entrance into the potters industry of those who are congenitally disposed to it."(Om82)

Stokinger and others have been particularly active in developing and promoting biological monitoring techniques aimed at detecting the hypersusceptible worker. In 1973 Stokinger reported five tests to detect genetic abnormalities. These abnormalities Stokinger and others suspect, could aggravate or compromise worker health in certain exposure situations. For example, sickle cell trait and sickle cell anemia might increase the risk to workers exposed to chemicals that deplete blood oxygen levels.

Certain immunological characteristics are speculated to indicate particular vulnerability to the sensitizing effects of isocyanates, while a reduced capacity to metabolize the compound tetraethylthiuram is believed to indicate an enhanced susceptibility to carbon disulfuide intoxication.

Stokinger argued that such tests were necessary to increase the degree of protection offered to workers:

> "...there is no provision in many, if not in most, industrial standards ... that assures protection of <u>all</u> workers; the hypersusceptibles commonly respond to exposures well below the limits set by the standards."(St73)

The whole question of pre-screening for hypersusceptibles has rather sinister implications. Firstly, it is not entirely certain what is meant by hypersusceptibility. Is there a definition which clearly defines hypersusceptible people or is the label applied to people who suffer workplace disease? The definition of hypersuscepibility is obviously not a purely scientific one. Nevertheless, as Schrecker notes:

> "...screening out potentially vulnerable workers is a strategy with few costs to industry other than the cost of testing itself."(Sc86)

Miller, in an article on the ethics and legality of screening for hypersusceptibles, concluded that:

> "...biological monitoring could ... be used to screen susceptible people from the work force at the outset. Employers are usually reluctant to hire workers, if they can avoid it, who can be predicted to cost them money in terms of future illness. Hiring policies could obviously be structured in accordance with the results of comprehensive pre-employment biological monitoring to achieve this end ...
>
> The most efficient way for management to maintain a healthy work force is to avoid hiring employees known to be susceptible to occupational illness...
>
> Biological monitoring offers management an extremely useful tool for predicting which employees constitute special risks for developing occupational disease."(Mi83)

The move toward biological monitoring in occupational health seems to be driven by insecurities about the existing, essentially judgemental systems for defining exposure limits and applying them as TWAs. Detection of hypersusceptibles would reassure that TLVs protect 'nearly all' workers and that those they do not protect are to some degree responsible for their own ailments because of genetic predisposition.

Further, biological monitoring which can relate internal levels of metabolites to observed physiologic effects could dispense with judgemental values about safe levels as well as the concerns about the scientific validity of TWA. Actually this 'ideal' is proving far more difficult than it sounds. There are sizeable practical problems to the detection of hypersusceptibles and the correlation of physiologic effects with levels of metabolites in body fluids.

However, it is not at all certain that the trend toward medical and biological monitoring of the worker will in any way produce an exposure setting system with better scientific foundations than TWA. ACGIH themselves note that:

> "...rapidly changing concentrations in body fluids complicate the interpretation of data and the average body burden of a chemical attained during a work shift can easily be over predicted or under predicted. Furthermore, biological measurements fail in most instances to detect transient periods of over-exposure during the work shift."(Do84)

So far, reliable biological monitoring techniques are claimed for only a few chemicals. Much of the concerns expressed against biological monitoring point out that the biological indicators tend to serve as a substitute rather than as a supplement to airborne exposure limits. Medical monitoring shifts the emphasis from preventing adverse health effects to detecting them, an approach raises considerable ethical questions.

The situation regarding scientific validity for radiation protection shows some similarities and some differences. Firstly, concerns about scientific validity do not seem to be as evident in health physics as they are in occupational toxicology. However, the science underlying the system of radiation protection for internal radiation exposures seems to be as uncertain as that underlying occupational toxicology. A fundamental concept in ionizing radiation is that delayed effects of radiation (cancer, genetic effects shortening of life span, and cataracts) may be caused by a single large overexposure or by continuing low level overexposure. To put it another way, detrimental effects depend on total accumulated dose and are independent of dose rate. The underlying assumption of this principle is that there is no biological repair of low dose rate, long-term ionizing radiation induced injury. This fundundamental assumption does not appear to have received substantial scientific validation, yet it underlies radiation protection in much the same way that 'CT equals constant toxicological effect' underlies occupational chemical exposure protection. There are, however, important differences in the significance of scientific uncertainties in occupational health and health physics. It could be argued that validation of the assumptions about the absence of biological repair in health physics really do not matter since the assumption reflects a worst case senario. Error in the assumption would not adversely affect those exposed. This is not so for occupational health where the incorrect assumption that CT is a constant could clearly produce adverse effects in those exposed.

Further, the whole system of radiation protection focuses on dose even though there is no direct method for actually measuring what a whole body or body organ 'tolerance dose' might be. The standard of 5 rems per year is a judgemental value based on the absence of any noted effects in humans. The vast majority of other figures used in health physics are calculated values derived or extrapolated from the application of theoretical models. Such models are developed from often tenous data about human chemical metabolism.

These points, reflecting in certain areas a lack of underlying scientific validity, do not seem to have overtly concerned those involved in health physics. However, health physics shows a remarkable and striking emphasis on the development of models, concepts and derived values. Professionals in the field of health physics acknowledge that some underlying principles of radiation protection need refinement because scientific validation is difficult or impossible. Scientific efforts in these difficult areas have focused on a sort of 'second order' or 'trans science' activity which develops, with enormous sophistication and detail, models for data extrapolation. The application of such models and concepts has resulted in a sizeable proliferation of derived value standards. The fact that these numbers cannot be scientifically verified is rarely mentioned in the literature.

Perhaps in health physics, as in occupational health, there is the feeling that numbers have a certain authority. To some degree, the existence of numbers tends to imply that the science behind them is sound and secure.

This point was noted in 1971 when the NCRP issued a report entitled "Basic Radiation Protection Criteria". Taylor comments that throughout the drafting of this report:

> "...there was increasing concern on the part of the council about the growing complexity in the numerical expression of standards that seem to imply a better basic knowledge about the subject than actually existed."

Certainly the situation which caused NCRP concern in 1971 seems to be greatly magnified in 1986.

In health physics, there is no evidence of a trend towards medical monitoring as a search for scientific validation. Indeed medical monitoring in health physics is kept firmly where it should be and has not been allowed to stray into the realm of a "control" program. According to ICRP 26:

> "...medical surveillance has no part to play in the effectiveness of a radiation protection program."

It is worth reflecting that since controlled exposure to ionizing radiation is kept below 5 rem/year, the detriment is solely in late occurring neoplasms. Signs and symptoms of physiological or behavioural effects would not be expected - a quite dissimilar stiuation from occupational chemical exposures.

However, it is interesting to speculate that perhaps the intense activity on concepts, models, and derivations is health physics' attempt to seek firmer scientific foundations. An old Eastern European maximum, used in scientific circles, states that:

> "...there is nothing as practical as a good theory."

Could it be that health physics is in search of a good theory on which to base its practice? The many volumes of ICRP seem to suggest so.

Taylor notes that:

> "...it is interesting to realize that because radiation as a toxic agent has been studied longer than most other such agents attempts at sophistication of the understanding of the problem have led to the adoption of concepts for which there are, even today, no complete biological bases."(Ta71)

There is no documentation in occupational health toxicology that can be remotely compared with the extensive documentation of the NCRP or ICRP. Occupational health toxicology still searches for some scientific basis for its exposure limits and their application. Health physics makes the best of what little science is available and strides boldly in areas of data extrapolation where occupational toxicology fears to tread.

21.0 CONCLUSIONS

When comparing the rationales for standard setting between the ten chemicals chosen and ionizing radiation, initial impressions are somewhat deceiving. The enormous documentation of ICRP, NCRP and other organizatins in the radiation protection field contrast markedly with the dearth of information about the toxicity of chemicals.

One is apt to conclude that the differences in the standard setting system can be traced solely to a wide disparity in the knowledge base for ionizing radiation versus chemicals. Logically we would expect this to be the case. Ionizing radiation is a relatively homogenous entity, comparatively well studied for its adverse effects on biological tissue. Chemicals on the other hand are both numerous and hetrogenous in their nature. Mankind's knowledge about most of these chemicals does not approach his knowledge about the health effects of ionizing radiation.

In 1984, an expert panel of the U.S. National Academy of Sciences conducted a review of the available knowledge concerning the toxicology of chemicals. This review was carried out at the request of the U.S. National Toxicology Program. The report stated that:

> "...that the amount of information available about chemicals can be correlated with the degree of federal regulation."

Radiation has always been heavily regulated and this, in part, may be responsible for the extensive documentation on ionizing radiation that exists in publications such as those by the NCRP, ICRP and others. As far as chemicals are concerned, drugs have been the most adequately tested while chemicals in industry are generally studied the least. Of the 53,000 commercially important chemicals reviewed by the U.S. National Academy of Sciences, only a few had been subjected to extensive toxicity testing. NAS reported that they could find no toxicity data for about 80 per cent of 49,000 chemicals in the study and those 49,000 excluded pesticides, drugs, cosmetics and food additives.

However, early impressions do not bear close scrutiny. Disparities in knowledge are not the only basis for differences in the standard setting systems. Inspection of the voluminous

literature on ionizing radiation protection standards belies initial impressions. At the very fundamental level there are distinct similarities in the problems for setting workplace radiation and chemical protective standards. In fact, it could be argued that there are many similarities in what is unknown. The differences in the standard setting systems do not solely reflect disparities in the knowledge base but rather differences in approaches aimed at dealing with distinctly similar problems.

Ionizing radiation is a "toxic" agent, and like the other ten toxic agents discussed in this report, the experimental determination of the dose or exposure that will not cause any biological harm is impossible. Existing experimental procedures cannot scientifically validate a dose or an exposure level which will unequivocally protect against chronic disease.

Not only is it impossible to determine a threshold dose or exposure, but it is out of the realm of science to determine even if a threshold dose exists at all. This is true for all of the ten chemicals discussed as well as for ionizing radiation and is the basic dilema for both occupational toxicology and health physics.

In the absence of scientific evidence, occupational toxicology has opted for a professional judgement system which juggles the health consequences of overexposure with the costs to industry of maintaining stringent controls. Health physics also uses a professional judgement system for establishing standards but ICRP does not seem greatly concerned with balancing its recommended standards against the economic or technical feasibility of implementing them at the practical level. In this respect ICRP seems to assume a role more akin to that of NIOSH than ACGIH.

In occupational toxicology the use of professional judgement to determine safe levels (and the obvious compromises that these judgements undergo to accomodate economic considerations) has led to considerable disquiet about the exposure standards that are used.

Not only is there an absence of good scientific validity for the numbers chosen but the way many of these numbers are implemented (by using workplace time-weighted averages) also raises concerns. Time-weighted average is not a scientifically validated concept.

As in occupational toxicology, health physics has underlying concepts which cannot be scientifically validated. The idea that detrimental effects are caused by total accumulated dose independent of dose rate, has no concrete foundation in scientific experimentation because the underlying assumptions regarding lack of biological repair have not been validated. This is not a serious problem in health physics since it is a 'worst case' assumption. However, the application of radiation protective principles in the workplace is not without its ambiguities. Although the emphasis is on permissible doses to the body and organs, doses cannot be directly measured. They are standards derived from a level judged to be safe when accumulated by the whole body. Further, these doses cannot be directly measured in the workplace, but rather are obtained and deduced from measurements of exposure. This could almost be considered a sleight of hand system, but again, its significance is minimal since in the controlled environment ionizing radiaton levels would not be expected to cause any noticeable short-term effects..

As with occupational toxicology, health physics shows uncertainties in some aspects of the scientific validity for its underlying principles as well as for its practical implementation in the workplace.

Perhaps the concern about scientific validation is merely academic. Protection in both fields is a practical problem which must obtain resolutions despite the absence of firm scientific foundations. Both fields have developed theories and both exercise some degree of professional judgement in order to facilitate practical protective guidelines and policies. Theories are used as a means of addressing practical problems in the absence of better scientific knowledge. Perhaps the greatest misdemeanor in the area of occupational toxicology is the absence of any admission that theories, rather than hard science lie behind the standard setting and protective system. It is possible that ACGIH feels that the credibility and authority of its standard setting would be diminished by the admission that it is not backed up by hard science.

Interestingly, health physics has a heavily theoretical component and makes no apparent attempt to hide this fact. However, it might be argued that the heavy emphasis on models and derivations gives the illusory image of a scientifically well-founded discipline. It is also worth remarking that perhaps the large theoretical component to health physics has

flourished because in controlled environments the consequences of errors in theoretical assumptions are unlikely to cost lives or cause serious morbidity. This is not so in occupational toxicology where theoretical modeling is largely shunned since the consequences of error, even in controlled environments could be catastrophic.

It is difficult to know or suggest ways in which either field of protection could improve or develop better bases for standard setting. Concerns about scientific validity have driven occupational toxicology more and more towards the medical monitoring system, while health physics seems to be preoccupied with defining new concepts and new theories. Both these efforts represent attempts by professionals in their respective areas to develop better bases for their protective standards and practices. This leads to a critical analysis of the control on the standard setting systems which is exacted through the members of ACGIH and ICRP. In both fields there is what we might call "professional sovereignty". That is to say, those with knowledge in the field have a jurisdiction over evaluating pertinent data and arriving at judgemental values which form the basis for the standards. The difficulty with a professional sovereignty system is that the people who decide on the standards are rarely found in the population that has to work by those standards. The work force, those people most effected by the standards have little or no input into what those standards should be or how they are implemented. In other words, not only do the systems of radiation protection and workplace chemical protection, as practiced by ICRP and ACGIH, lack scientific validity in some areas, but they have no social validity either.

In occupational health, this problem has been recognized and is currently addressed by a number of jurisdictions, most noteably that of the Ontario Ministry of Labour. This department appreciates that since exposure limits and their implemention are based on judgemental values, then those people who are affected by the standards ought to be a part of the process of setting and implementing them. This view is apparently shared by the Atomic Energy Control Board (AECB) which, since 1980, has practiced a consultative system.

The Ontario Ministry of Labour and the AECB reflect the growing recognition, in their respective fields, that standard setting and workplace health practice implementation is as much a social as it is a scientific activity. Public and labour input into standard setting and protective policies would seem to be

an essential pre quisite for public confidence in, and acceptance of, the decision making systems. If there are advances to be made in occupational health and health physics standard setting processes, then they should be made in the area of improving the social validity of those standards. Many aspects of the scientific validity are as yet out of our reach.

22.0 REFERENCES

Ab76 Abbritti, G.; Siracusa, A.; Cianchetti, C.; Coli, C.A.; Curradi, F.; Perticoni, G.F.; DeRosa, F. Shoemakers' neuropathy in Italy : the aetiological problem. British Journal of Industrial Medicine. Vol. 33 (1976). p. 92-99

Ac84 American Conference of Governmental Industrial Hygienists Inc. Toluene-2,4-diisocyanate. In: Documentation of the threshold limit values. 4th edition. Cincinnati, Ohio, 1980. p. 403.1-403.6

Ad52 Adams, E.M.; Spencer, H.C.; Rowe, V.K. et al. Vapour toxicity of carbon tetrachloride determined by experiments on laboratory animals. A.M.A. Archives of Industrial Hygiene and Occupational Medicine. Vol. 6 (1952). p. 50-66

Ad69 Adams, R.G.; Harrison, J.F.; Scott, P. The development of cadmium-induced proteinuria, impaired renal function and osteomalacia in alkaline battery workers. Q J Med. Vol. 38 (1969). p. 425-442

Ad75 Adams, W.G.F. Long-term effects on the health of men engaged in the manufacture of toluene diisocyanate. British Journal of Industrial Medicine. Vol. 32 (1975). p. 72-78

At85 Atherley, G. A critical review of time-weighted average as an index of exposure and dose, and of its key elements. American Industrial Hygiene Association Journal. Vol. 46 (1985). p. 481-487

Ba28 Barclay, A.E.; Cox, S. Radiation risks of the roentgenologist. Amer. J. Roentgen. Vol. 19 (1928). p. 551-561

Ba52 Baader, E.W. Chronic cadmium poisoning. Industrial Medical Surgery. Vol.21 (1952). p. 427-430

Ba54 Barsotti, M. (Stenocardiac attacks in workers engaged in the manufacture of dynamites containing nitroglycerol). Med Lavoro. Vol. 45 (1954). p. 544-548

Be30 Behnken, H. Dosimetrische Untersuchungen uber Roentgenstrahlenschutz and strahlenschutzrohren. Fortschr. Geb. Roentgenstr. Vol. 41 (1930). p. 245-256

Be66 Beton, D.G.; Andrews, G.S.; Davies, H.J.; Howells, L.; Smith, G.F. Acute cadmium fume poisoning : five cases with one death from renal nacrosis. British Journal of Industrial Medicine. Vol. 23 (1966). p. 292-300

Be69 Berlin, M.; Nordberg, G.F.; Serenios, F. On the site and mechanism of mercury vapor resorption in the lung. Arch. Env. Health. Vol. 18 (1969). p. 42-50

Be82 Bernstein, I.L. Isocyanate induced pulmonary diseases : a current perspective. Journal of Allergy and Clinical Immunology. Vol. 70, no. 1 (1982). p. 24-31

Bi51 Bidstrup, P.L.;. Bonnel, J.A.; Harvey, D.G. et al. Chronic mercury poisoning in men repairing direct current meters. Lancet. Vol. 2 (1951). p. 856-861

Bi56 The Biological effects of atomic radiation - a report to the public. Washington : U.S. Government Printing Office, 1956

Bo40 Bowdipch, M.; Drinker, K.P.; Haggard, H.H.; Hamilton, A. Code for safe concentrations of certain common toxic substances used in industry. The Journal of Industrial Hygiene and Toxicology. Vol. 22 (1940). p. 251

Bo59 Bonnell, J.A.; Kazantzis, G.; King, E. A follow-up study of men exposed cadmium oxide fume. British Journal of Industrial Medicine. Vol. 16 (1959). p. 135-147

Bo73 Bohlen, P.; Schlunegger, U.P.; Lauppi, E. Uptake and distribution of n-hexane in rat tissues. Toxicology and Applied Pharmacology. Vol. 25 (1973). p. 242-249

Br76 Brewis, R.A.L. In: Lecture notes on respiratory disease. London : Blackwell Pub., 1976

Br77 Bruckner, J.V.; Peterson, R.G. Toxicology of aliphatic and aromatic hydrocarbons. National Institute of Drug Abuse Research Monograph-Serial. Vol. 15 (1977). p. 124-163

Br80 Brognone, F.; Perbellini, L.; Grafluri, E. et al. Biomonitoring of industrial solvent exposures in workers alveolar air. Int. Arch. Occup. Environ. Health. Vol. 47 (1980). p. 245-261

Br84 Bruce, A. Chronic poisoning by bisulfide of carbon. Edinburgh Medical Journal. Vol. 29 (1884). p. 1009-1014

Br84 Brawn, J.; Stoss, H.; Zober, A. Intoxication following the inhalation of hydrogen fluoride. Archives of Toxicology. Vol. 56 (1984). p. 50-54

Bu73 Burke, W.J.; Hoegg, U.R.; Phillips, R.E. Systemic fluoride poisoning resulting from a fluoride skin burn. Journal of Occupational Medicine. Vol. 15 (1973). p. 39-41

Bu76 Butcher, B.T.; Salvaggio, J.E.; Weill, H.; Ziskind, M.M. Toluene diisocyanate (TDI) pulmonary disease : immunologic and inhalation challenge studies. Journal of Allergy and Clinical Immunology. Vol. 58 (1976). p. 89-100

Bu77 Butcher, B.T.; Jones, R.N.; Neill, C.E. et al. Longitudinal study of workers employed in the manufacture of toluene diisocyanate. American Review of Respiratory Dieseases. Vol. 116 (1977). p. 411-421

Bus77 Bus, J.S.; White, E.L.; Barrows, C.S. Disposition of n-hexane in rats after single and repeated inhalation exposure. Toxicology and Applied Pharmacology. Vol. 48 (1977). p. A167

Cc85 Hydrogen fluoride. Hazard summary no. 8. Hamilton, Ontario : CCOHS, 1985

Ch28 Chantraine, H.; Profitlich, P. Uber den schutz den Artzes und seiner gehilfen vor den Roentgenstrahlen. Forschr. Geb. Roentgenstr. Vol. 38 (1928). p. 121-128

Ch77 Chang, L.W. Environ. Res. Vol. 14 (1977). p. 329

Ch85 Cherian, M.G.; O'Heny, J.; Kusiak, R.A. Health effects of cadmium and its inorganic compounds. Health Studies Service for the Ontario Ministry of Labour, May 1985. p. 44-46

Co45 Cook, W.A. Maximum allowable concentrations of industrial atmospheric contaminants. Industrial Medicine. Vol. 14 (1945). p. 936-946

Co50 Committee on chemical agents report of panel on environmental agents 9th annual congress of industrial hygiene, Chicago, January 1949. Archives of Industrial Hygiene and Occupational Medicine. Vol. 1 (1950). p. 601-624

Co59 A Commentary on the report of the United Nations Scientific Committee on the effects of atomic radiation - report II of the Committee on Pathologic Effects of Atomic radiation, Pub. 647. Washington : U.S. Government Printing Office, 1959

Co69 Cook, W.A. Problems of setting occupational exposure standards --- background. Archives of Environmental Health. Vol. 19 (1969). p. 272-276

Co71 Coates, E.O., Jr.; Watson, J.H.L. Diffuse interstitial lung disease in tungsten carbide workers. Ann. Intern. Med. Vol. 75 (1971). p. 709

Co73 Coates, E.O., Jr. Hypersensitivity bronchitis in tungsten carbide workers. Chest. Vol. 63 (1973). p. 390

Cr74 Creech, J.L.; Johnson, M.N. Angiosarcoma of liver in the manufacture of polyvinyl chloride. J. Occup. Med. Vol. 16 (1974). p. 150-151

De63 Derryberry, O.M.; Bartholomew, M.D.; Fleming, R.B.L. Fluoride exposure and worker health. Archives of Environmental Health. Vol. 6 (1963). p. 503-514

De78 Delorme, F.; Teriault, G. Ten cases of angiosarcoma of the liver in Shawinigan, Quebec. J. Occup. Med. Vol. 20 (1978). p. 338-340

De86 Deichmann, W.B.; Henschler, D.; Holmstedt, B.; Keil, G. What is there that is not poison? A study of the third defense by Paracelsus. Archives of Toxicology. Vol. 58 (1986). p. 207-213

Di62 Dieffenbacher, P.F.; Tompson, J.H. Burns from exposure to anhydrous hydroflouric acid. Journal of Occupational Medicine. Vol. 4 (1962). p. 325-326

Do84 Documentation of threshold limit values. Cincinnati, Ohio : ACGIH, 1980 (with supplemental information through 1984)

Do86 Documentation of TLVs. Vinyl chloride. Cincinnati, Ohio : ACGIH, 1986

Du76 Duck, B.W.; Carter, J.T. Vinyl chloride and mortality? The Lancet. Vol. 2 (1976). p. 195

Ed96 Edison, T.A. et al. Effect of x-rays upon the eye. Nature. Vol. 53 (1896). p. 421

El48 Elkins, H.B. Case for maximum allowable concentrations. American Industrial Hygiene Association Quarterly. Vol. 9 (1948). p. 22-25

El59 Elkins, H.B. Chemistry of industrial toxicology. 2nd ed. New York : Wiley, 1959. p. 167

Ev66 The Evaluation of Risks from Radation (ICRP Pub. 8). A Report Prepared by a Task Group of Committee 1 of the International Commission on Radiological Protection. Health Phys. Vol. 12 (1966). p. 239-302

Ev81 Evans, R.D. Inception of standards for internal emitters, radon and radium. Health Physics. Vol. 41 (1981). p. 437-448

Eve66 Eve, I.S. A review of the physiology of the gastrointestinal tract in relation to radiation doses from radioactive materials. Health Physics. Vol. 12 (1966). p. 131

Fl31 Flurry, F.; Zernik, F. Schadliche Gase. Berlin, 1931. p. 453

Fr48 Frieberg, L. Proteinuria and kidney injury among workmen exposed to cadmium and nickel dust. Journal of Industrial Hygiene and Toxicology. Vol. 30 (1948). p. 32-36

Fr50 Frieberg, L. Health hazards in the manufacture of alkaline accumulators with special reference to chronic cadmium poisoning. Acta Med Scand. Vol. 240, supple. 138 (1950). p. 1-24

Fr74 Frieberg, L.; Piscator, M.; Nordberg, G.; Jellstrom, T. Cadmium in the environment. 2nd edition. Cleveland : CRC Press, 1974

Fr79 Frieberg, L.; Nordberg, G.; Bouk, V.D. eds. Elsevier/New York, 1979. p. 355-377

Ga43 Gafafer, W.M. Manual of industrial hygiene and medical science in all industries. Philadelphia, 1943. p. 508

Ge79 Gehring, P.T.; Watanabe, P.G.; Park, C.N. Risk of angiosarcoma in workers exposed to vinyl chloride as predicted from studies in rats. Toxicology and Applied Pharmacol. Vol. 49 (1979). p. 15-21

Ge85 Gee, J.B.; Morgon, W.K.C. A 10 year follow-up study of a group of workers exposed to isocyanates. Journal of Occupational Medicine. Vol. 27, no. 1 (1985). p. 15-18

Gl29 Glocker, R.; Reuss, A. Strahlenschutzmessunge. Fortschr. Geb. Roentgenstr. Vol. 40 (1929). p. 501-507

Go40 Gordie, S.T.; Trimber, M. Carbon disulfide poisoning : report of 21 cases. Industrial Medicine. Vol. 9 (1940). p. 232-234

Go73 Goldwater, L.J. Discussion, Chapter 1. In: Miller, M.W.; Clarkson, T.W. eds. Mercury, mercurials and mercaptans. Springfield : Charles C. Thomas, 1973. p. 19

Gr26 Greenburg, L. Benzol poisoning as an industrial hazard. Public Health Report. Vol. 41 (1926). p. 1516, 1537

Gr49 Grubbé, E.H. X-ray treatment, its origin, birth and early history. St. Paul, Minn. : Bruce Pub. Co., 1949

Gr81 Graham, W.G.B.; Debuc, O'Grady, R.V. Pulmonary function loss in Vermont granite workers. A long-term follow-up and critical reappraisal. Amer. Rev. Resp. Dis. Vol. 123, no. 1 (1981). p. 25-28

Gr83 Grandjean, P.; Thomsen, G. Reversibility of skeletal fluorosis. British Journal of Industrial Medicine. Vol. 4 (1983). p. 456-461

Ha47 Hardy, H.L.; Skinner, J.B. The possibility of chronic cadmium poisoning. Journal of Industrial Hygiene and Toxicology. Vol. 29 (1947). p. 321-324

Ha62 Hatch, T.F. Changing objectives in occupational health. American Industrial Hygiene Association Journal. Vol. 23 (1962). p. 1-7

Ha81 Hatch Associates Limited. Cadmium and its compounds. Health impact of production and usage in the workplace. Contract to the standards and programs branch, occupational health and safety divison. Toronto : Ontario Ministry of Labour, November, 1981

Ha84 Halton, D.M.; Baynes, C.H.; Dranitsaris, P. Toxicity levels to humans during acute exposure to hydrogen fluoride. A report prepared for the Atomic Energy Control Board, Ottawa, Ontario, Canada, INFO-0143, November 28, 1984

He27 Henderson, Y.; Haggard, H. Noxious gases and the principles of respiration influencing their action. American Chemical Society Monograph. Series No. 35. New York Chemical Catalog Co, 1927

He43 Henderson, Y.; Haggard, H.W. Noxious gases and the principles of respiration influencing their action. 2nd edition. New York : Reinhold Publishing, 1943

He62 Henschler, D; Assmann, W.; Meyer, K. The toxicology of toluene diisocyanates. Archive fur toxikologie. Vol. 19 (1962). p. 364-387

He71 Herskowitz, A.; Ishii, M.; Schaumburg, H.H. n-Hexane neuropathy : a syndrome occurring as a result of industrial exposure. New England Journal of Medicine. Vol. 285 (1971). p. 82-85

He73 Hernberg, S.; Nordman, C.H.; Samari, P. Coronary heart disease among workers exposed to carbon disulfide. British Journal of Industrial Medicine. Vol. 28 (1970). p. 313-325

He81 Henschler, D. Recent developments in assessing occupational exposures and health risks in western European countries. In: International Seminar. Assessment of Intoxications at the Workplace -- Roles of Ambient and Biological Monitoring, Luxembourg, 8-12 December 1980 Brussels: Commission of the European Communities, 1981

Hy80 Hygienic guide series. American Industrial Hygiene Association Journal. Vol. II (June 1980)

Ia76 IARC. Monographs on the evaluation of the carcinogenic risk of chemicals to man. Vol. 11 (1976). p. 64

Ia79 IARC. Monographs on the evaluation of the carcinogenic risk of chemicals to man. Vol. 19 (1979). p. 377-438

In28 International X-ray and Radiation Protection Committee, X-ray and radium protection. Brit. J. Radiol. (N.S.). Vol. 1 (1928). p. 358-363

In69 Inoue, T.; Eimatta, S.; Mivagaki, H.; Takeucki, Y. Presentation at the XVI congress on occupational health. Tokyo, September 22-27, 1969

Iw83 Iwata, M.; Takevchi, Y.; Hisanaga, N. et al. A study on biological monitoring of n-hexane exposure. Int. Arch. Occup. Environ. Health. Vol. 51 (1983). p. 253-260

Ja69 Jamamura, Y. n-Hexane polyneuropathy. Folia, Psychiatrica Neurologica Japonica. Vol. 23 (1969). p. 45-47

Ja80 Jacobi, W.; Eisfeld, K. Doses to tissues and effective dose equivalent by inhalation of Ra-222, Rn-220 and their short-lived daughters. Gesf. Strahen-und Umweltforshung. GSF Report 5-26. Munchen, 1980

Jag80 James, A.C.; Greenhalgh, J.F.; Birchall, A. A dosimetric model for tissues of the human respiratory tract at risk from inhaled radon and thorium daughters. Proceedings of 51st International Congress IRPA. Jerusalem, Israel. Vol. 2. Oxford : Pergamon Press, 1980

Jo81 Jorgensen, N.K.; Cohr, K.H. n-Hexane and its toxicologic effects : a review. Scandinavian Journal of Work, Environment and Health. Vol. 7 (1981). p. 157-168

Ka15 Kaye, G.W.C. X-rays. 2nd ed. London : Longmans, Green, 1915. p. 264

Ka26 Kaye, G.W.C. X-rays. 4th ed. London : Longmans, Green, 1926

Ka63 Kazantzis, G.; Flynn, F.V.; Spowage, J.S.; Trott, D.G. Renal tubular malfunction and pulmonary emphysema in cadmium pigment workers. Q J Med. Vol. 32 (1963). p. 165-192

Ka79 Karol, M.H.; Sandberg, T.; Riley, E.J.; Alarie, Y. Longitudinal study of tolyl-reactive IgE antibodies in workers hypersensitive to TDI. Journal of Occupational Medicine. Vol. 21, no. 5 (1979). p. 354-358

Ka86 Karol, M.H. Respiratory effects of inhaled isocyanates. In: Goldberg, L., ed. Critical review in toxicology. Vol. 16, issue 4. Boco Raton, Florida : CRC Press, 1986. p. 349-397

Ke82 Kee, M.M. Health standards and standard setting in the United States. Annals of the New York Academy of Sciences. Vol. 200 (1982). p. 707-711

Ki67 Kipling, M.D.; Waterhouse, J.A.H. Cadmium and prostatic cancer. The Lancet. Vol. 1 (1967). p. 730-731

Kl55 Klauder, J.V.; Shelanski, L.; Gabriel, K. Industrial uses of compounds of fluorine and oxalic acid. Archives of Industrial Health. Vol. 12 (1955). p. 412-419

Ko12 Kobert, R. Kompendium der praktischen Toxikologi zum Gebrauch fur artze, Studierende und medizinal bemte : Stutgard, 1912. p. 45

La10 Laws, C.F. Nitgroglycerol head. Journal of the American Medical Association. Vol. 54 (1910). p. 793

La45 Lauwerys, R.R.; Buchet, J.P.; Roels, H.A. Epidemiological survey of workers exposed to cadmium. Archives of Environmental Health. Vol. 28 (1974). p. 145-148

La61 Largent, E.J. Fluorosis. Ohio State University Press, Columbus, OH (1961)

La72 Lange, R.L.; Reid, M.S.; Tresh, D.D. et al. Non atheromatous ischemic heart disease following withdrawl from chronic industrial nitroglycerin exposure. Circulation. Vol. 46 (1972). p. 666

La73 Langham, W.H.; Healy, J.W. Maximum permissible body burdens and concentrations of plutonium : biological basis and history of development. In: Hodge, H.C.; Stannard, J.N.; Hursh, J.B., eds. Uranium, plutonium, transplutonic elements. New York : Springer Verlag, 1973. p. 569-592

La73 Lauwerys, R.R.; Buchet, J.P. Occupational exposure to mercury vapors and biological actions. Arch. Environ. Health. Vol. 27 (1973). p. 65-68

La77 Lauwerys, R. Evaluation of impact of cadmium on the health of man. Luxumberg : Commission of the European Communities, 1977. p. 72-74

La78 Lauwerys, R.; Stanescu, D.; Roeles, H.; Buchet, J.P. Proceedings of the first international cadmium conference. London : Metal Bulletin Limited, 1978. p. 201-204

Le11 Lehmann, K.B. Experimental studies of technically and hygenically important vapours of the organism (XV1-XX111). The chlorinated hydrocarbons of the aliphatic series in addition to observation regarding the single phase and two-phase toxicity of volatile substances. Archive Fur Hygiene und Baktariologie. Vol. 74, no. 1 (1911). p. 1-60

Le38 Lehmann, K.B.; Flurry, F. Toxikologie und hygiene der technischen Losungmittel. Berlin, 1938

Le67 Leidel, N.A. et al. Environmental and medical survey, Blockson Works, Olin Mathieson, Corp. DHEW, PHS Occupational Program (September 1967)

Le72 Lewis, G.P.; Coughlin, L.; Lusko, W.; Hartz, S. Contribution of cigarette smoking to cadmium accumulation in man. Lancet. Vol. 1 (1972). p. 291-292

Le74 Levinson, C. Work hazard : vinyl chloride. Basle : I.C.F., 1974. p. 20

Li75 Lilis, R.; Anderson, H.; Nicholson, W.J.; Daun, S.; Fishbein, A.S.; Selikoff, I.J. Prevalence of disease among vinyl chloride and polyvinyl chloride workers. Ann. N.Y. Acad. Sci. Vol. 246 (1975). p. 22-41

Lo82 Louch, W.J. The regulation of chemical exposure. Presented to Canadian Unionn of Public Employees, Montreal 1982. Hamilton, Ontario : CCOHS (D82-5E), 1982

Ma34 Machle, W.; Thamann, F.; Kitzmiller, K.; Cholak, J. The effects of the inhalation of hydrogen fluoride : I : response following exposure to high concentrations. Journal of Industrial Hygiene. Vol. 15 (1934). p. 129-145

Ma60 Mastromatteo, E.; Fisher, A.M.; Christie, H. et al. Acute inhalation toxicity of vinyl chloride to laboratory animals. Am. Ind. Hyg. Assoc. J. Vol. 21 (1960). p. 394-398

Ma63 Mayer, L.; Guelich, J. Hydrogen fluoride inhalation and burns. Archives of Environmental Health. Vol. 7 (1963). p. 71-73

Ma68 Magos, L. Uptake of mercury by the brain. Brit. J. Ind. Med. Vol. 25 (1968). p. 315-318

Ma75A Materne, D.; Lauwreys, R.; Buchet, J.P. et al. Investigations of the risks resulting from exposure to cadmium in two production plants and two plants using cadmium. Cahiers med trav. Vol. 12 (1975). p. 3-76

Ma75B Maltoni, C. The value of predictive experimental bioassays in occupational and environmental carcinogenesis : an example : vinyl chloride. Ambio. Vol. 4, no. 1 (1975)

Ma81 Mackison, F.W.; Stricoff, R.S.; Partridge, L.J. Jr., eds. Occupational health guideline for n-hexane. In: Occupational health guidelines for chemical hazards (NIOSH publication no. 81-123). Washington, D.C. : NIOSH, 1981

Mac85 MacKinnon, M.A. Director Medical Services, Allied Chemical, Amherstburg, Ontario - Personal communication, 1985

Mc46 McConnel, W.J. et al. Occupational medicine. Vol. 1 (1946). p. 551

Me56 Medical Research Council. The hazards to man of nuclear and allied radiations. Cmd 9780. H.M.S. Office, 1956

Mi67 Miyagaki, H. Electrophysiological studies of the peripheral neurotoxicity of n-hexane. Japanese Journal of Industrial Health. Vol. 9 (1967). p. 660-671

Mi75 Miller, A.; Teirstein, A.S.; Chuang, M.; Selikoff, I.J.; Wasshaw, R. Changes in pulmonary function in workers exposed to vinyl chloride and polyvinyl chloride. Ann. N.Y. Acad. Sci. Vol. 246 (1975). p. 42-52

Mi83 Miller, F.H. Biological monitoring : the employer's dilema. American Journal of Law and Medicine. Vol. 94 (1983). p. 387-426

Mo75 Morton, W.K.C.; Seaton, A. Occupational lung diseases. Philadelphia : W.B. Saunders, 1975. p. 244-247

Mo75 Morgan, K.C.; Seaton, A. Silicosis. In: Occupational lung disease. Chapter 7. Philadelphia : W.B. Saunders, 1975. p. 80-111

Mo80 Regulation respecting isocyanates - made under the Occupational Health and Safety Act. Toronto : Ontario Ministry of Labour, 1980

Mo82 Mosaic of Mosaics. Hamilton, Ontario : CCOHS, 1982

Mu25 Mutscheller, A. Physical standards of protection against roentgen ray dangers. Amer. J. Roentgen. Vol. 13 (1925). p. 65-70

Na56 National Research Council. The biological effects of atomic radiation - summary reports. Washington : National Academy of Sciences-National Research Council, 1956

Ne43 Nelson, K.W.; Enge, J.F. Jr.; Ross, M.; Woodman, I.E.; Silverman, L. Sensory response to certain industrial solvent vapours. Journal of Industrial Hygiene and Toxicology. Vol. 25 (1943). p. 282-285

Ne57 Neumann, H.H. The milk and water intake of small children. Archives of Pediatrics. Vol. 74 (1957). p. 456-462

New21 Newman, B.J.; McConnell, W.J.; Spencer, O.M.; Phillips, F.M. Lead poisoning in the pottery trades. Public Health Bulletin No. 116 (1921)

Ni42 Nicaud, P.; Lafitte, A.; Gros, A. Les troubles de l'intoxication chronique par le cadmium. Archives nal prof. Vol. 5 (1942). p. 192-202

Ni50 Ninth annual congress on industrial health : report of the panel on environmental hygiene. Archives of Industrial Hygiene and Occupational Medicine. Vol. 1 (1950). p. 601-624

Ni73 NIOSH. Criteria for a recommended standard, occupational exposure to inorganic mercury. Washington : U.S. Government Printing Office, 1973

Ni73 NIOSH occupational exposure to toluene diisocyanate : criteria for a recommended standard. Washington, D.C. : U.S. Department of Health Education and Welfare, 1973

Ni74 Criteria for a recommended standard to vinyl chloride. Cincinnati, Ohio : NIOSH, 1974

Ni75 National Institute for Occupational Health and Safety. Criteria for a recommended standard - occupational exposure to crystalline silica. DHEW pub. no. (NIOSH) 75-120 (1975)

Ni76 NIOSH criteria for a recommended standard for occupational exposure to hydrogen fluoride. Cincinnati, Ohio : U.S. Department of Health, Education, and Welfare, Public Health Service Centre for Disease Control, March 1976

Ni77 NIOSH criteria for a recommended standard : occupational exposure to alkanes (C_5-C_8). DHEW (NIOSH) publication no. 77-151, 1977

Ni77 NIOSH criteria for a recommended standard - occupational exposure to carbon disulfide, DHEW (NIOSH) publication no. 77-156, 1977

Ni77 National Institute for Occupational Safety and Health. Criteria for a recommended standard : occupational chemical exposure to alkanes. NIOSH publication no. 77-151. Washington, D.C. : NIOSH, 1977

Ni78 NIOSH : criteria for a recommended standard : occupational exposure to nitroglycerine and ethylene glycol dinitrate, DHEW (NIOSH) publication no. 78-167, 1978

Ni85 Nielsen, J.; Sango, C.; Winroth, G.; Hallberg, T.; Skerfving, S. Systemic reactions associated with polyisocyanate exposure. Scandinavian Journal of Work, Environment and Health. Vol. 11 (1985). p. 51-54

Oa61 Oakberg, E.F.; Clark, E. Effect of dose and dose rate on radiation damage to mouse spermatogonia and oocytes as measured by cell survival. J. Cell. Comp. Physiol. Vol. 58, suppl. 1 (1961). p. 173-182

Ol02 Oliver, T., ed. Indian rubber : dangers incidental to the use of bisulfide of carbon of naphtha. In: Dangerous Trades. London : John Murray, 1902. p. 407-474

Om82 Omenn, G.S. Predictive identification of hypersusceptible individuals. Journal of Occupational Medicine. Vol. 24 (1982). p. 369-374

On81 Ontario Ministry of Labour, Occupational Health and Safety Division. Report on the designation of vinyl chloride in Ontario. Toronto : Ontario Ministry of Labour, August 27, 1981

On82 Assessment of worker exposure to isocyanates. United Technology and Science Inc. Report to Ontario Ministry of Labour, 1982

On82 Ontario Ministry of Labour, Occupational Health and Safety Division. Report on the designation of silica in Ontario. Toronto, Ontario : Ministry of Labour, 1982

Pa29 Patty, F.A.; Yant, W.P. Odour intensity and symptoms produced by commercial propane, butane, pentane, hexane and heptane vapour. Reprinted from the U.S. Bureau of Mines Investigation. No. 2979, 1929

Pa56 Pathologic effects of atomic radiation, pub. 452. Washington : U.S. Government Printing Office, 1956

Pa76 Patwardhan, J.R.; Finckh, E.S. Fatal cadmium-fume pneumonitis. Medical Journal of Australia. Vol. 1 (1976). p. 962-966

Pe68 Peters, J.M.; Murphy, R.L.H.; Pagnotto, L.D.; Van Ganse, W.F. Acute respiratory effects in workers exposed to low levels of toluene diisocyanate TDI. Archives of Environmental Health. Vol. 16 (1968). p. 642-647

Pe69 Peter, J.M.; Murphy, R.L.H.; Ferris, B.G. Ventilatory function in workers exposed to low levels of toluene diisocyanate : a six month follow-up. British Journal of Industrial Medicine. Vol. 26 (1969). p. 115-120

Pe80 Perbellini, L.; Brugnone, F.; Pavan, I. Identification of the metabolites of n-hexane, cyclohexane and their isomers in mens urine. Toxicol. Appl. Pharmacol. Vol. 53 (1980). p. 220-229

Pe81A Perbellini, L.; Brugnone, F.; Gafturi, E. Neurotoxic metabolites of "commercial hexane" in the urine of shoe factory workers. Clinical Toxicology. Vol. 18 (1981). p. 1377-1385

Pe81B Perbellini, L.; Brugnone, F.; Silvestri, R. et al. Measurement of the urinary metabolites of n-hexane, cyclohexane and their isomers by gas chromatography. Int. Archiv. Occupational Environmental Health. Vol. 48 (1981). p. 99-106

Pe81C Perbellini, L.; Brugnone, F.; Faggionato, G. Urinary excretion of the metabolite of n-hexane and its isomers during occupational exposure. Brit. J. Ind. Med. Vol. 38 (1981). p. 20-26

Pe86 Personal communication. Inspector's statement from the Occupational Health and Safety Divison, Ontario Ministry of Labour, Hamilton.

Pi79 Piscator, M. Metabolism and effects of cadmium. International Conference Management and Control of Heavy Metals in the Environment. London (1979)

Po22 Proceedings, Annual meeting of the American Roentgen Ray Society, September 1920

Po65 Potts, C.L. Cadmium proteinuria : the health of battery workers exposed to cadmium oxide dust. Annals of Occupational Hygiene. Vol. 8 (1965). p. 55-61

Re21 Recommendations of the British X-ray and Radium Protection Committee. British Journal of Radiology, 1921

Re59 Recommendations of the International Commission on Radiological Protection (Adopted September 9, 1958). ICRP Pub. 1, Pergamon Press, London, 1959

Re60 Recommendations of the International Commission on Radiological Protection (ICRP Pub. 2). Report of Committee II on Permissible Dose for Internal Radiation (1959). Health Phys. Vol. 3 (1960). p. 1-233

Re66 Recommendations of the International Commission on Radiological Protection (ICRP Pub. 10). Report of Committee 4 on Evaluation of Radiation Doses to body Tissues from Internal Contamination Due to Occupational Exposure, Pergamon Press, Oxford, 1968

Re77 Recommendations of the International Commission on Radiological Protection. Publication 25. Pergamon Press, 1977. paragraphs 60 and 104

Ri78 Riihimaki, V.; Pfaffli, P. Percutaneous absorption of solvent vapours in man. Scandinavian Journal of Work, Environment and Health. Vol. 4 (1978). p. 73-85

Ro02 Rollins, W. Vacuum tube burns. Boston Med. Surg. J. January 9, 1902

Ro03 Rollins, W. Notes on x-light. Boston, 1903. p. 290

Ro09 Ronzani, E. Experimental studies on the effect of inhaling irritant industrial gases upon the organisms defense mechanisms against infectious disease. Arch. f. Hyg. Vol. 70 (1909). p. 235-269

Ro86 Ross, J. Medical chronical : two cases of chronic poisoning by bisulfide of carbon. Vol. 5 (1886). p. 257-269

Ru29 Russell, A.E.; Britten, R.H.; Thompson, L.R.; Bloomfield, J.J. The health of workers in dusty trades, exposure to siliceous dust in the granite industry. Public Health Bulletin No. 187 (1929).

Ru77 Ruzzuto, N.; Terzian, H.; Goliazzo-Rizzuto, S. Toxic polyneuropathies in Italy due to leather cement poisoning in shoe industries. Journal of Neurological Science. Vol. 31 (1977). p. 343-354

Ry61 Rye, W.A. Proceedings of 13th international congress on occupational health, July 1860, p. 361-364 (1961)

Sa27 Sayers, R.R. Toxicology of gases and vapours. International Critical Tables of Numerical Data, Physics, Chemistry and Technology. Vol. 2. New York, 1927. p. 318-321

Sa29 Sayers, R.R., Yent, P. and Thomas, B.G.H.; Berger, L.B. Physiological response attending exposure to vapours of methyl chloride, ethyl bromide, and ethyl chloride. U.S. Public Health Service, Public Health Bulletin No. 185, 1929. p. 56

Sa35 Sayers, R.R; Dala valle, J.M. Prevention of occupational diseases other than those that are caused by toxic dust. Mechanical Engineering. Vol. 57 (1935). p. 230-234

Sa72 Sanockij, I.V. Methods used in the USSR for establishing biological safe levels of toxic substances : papers presented at a WHO meeting held in Moscow from the 12-19 December, 1972. Geneva : WHO, 1975

Sc47 Schrenk, H.H. Chief Health Division, Bureau of Mines, Pittsburgh. Interpretations of permissible limits. American Industrial Hygiene Association Quarterly. Vol. 8 (1947). p. 55-60

Sc78 Schmidt, C.W.; Metze, H. Hydrofluoric acid skin corrosion - review of 68 cases. Das Deutsche Gesundheitswesen, Berlin, German Democratic Republic. Vol. 33 (1978). p. 761-766

Sc86 Schrecker, T. Occupational exposure limits - a report for CCOHS, Hamilton, Ontario, 1986

Se74 Seppalainen, A.M.; Tolonen, M. Neurotoxicity of long-term exposure to carbon disulfide in the viscose rayon industry : a neurophysiological study. Scandinavian Journal of Work, Environment and Health. Vol. 11 (1974). p. 145-153

Sh74 Shirabe, T.; Tsuda, T.; Terao, A.; Araki, S. Toxic neuropathy due to glue sniffing. Journal of Neurological Science. Vol. 21 (1974). p. 101-113

Sm48 Smith, A.R.; Moskowitz, S. Urinary excretion of mercury. New York state department of labor monthly rev. Vol. 27 (1948). p. 45-47

Sm70 Smith, R.G.; Vorwald, A.J.; Patil, L.S. et al. Effects of exposure to mercury in the manufacture of chlorine. Am. Ind. Hyg. Assoc. J. Vol. 31 (1970). p. 687-700

So82 Sorahan, T. Mortality study of nickel cadmium battery workers. In: Wilson, D.; Volpe, R.A., eds. Cadmium 81. Longon : The Cadmium Association, 1982. p. 138-141

Sp68 Spiers, F.W. Radioisotopes in the human body. New York : Academic Press, 1968

Sp79 Spencer, P.S. Communication to TLV committee, 1979

Sp80 Spencer, P.S.; Schaumburg, H.H.; Sabri, M.I.; Veronesi, B. The englarging view of hexacarbon neurotoxicity. CRC Critical Reviews in Toxicology. Vol. 7 (1980). p. 279-355

St43 Sterner, J.H. Determining margins of safety : criteria for defining a "harmful" exposure. Industrial Medicine. Vol. 12 (1943). p. 514-518

St49 Stokinger, H.E. et al. Pharmacology and toxicology of uranium compounds, Chap. 17. NNES VI 2. McGraw Hill, New York (1949)

St52 Stone, R.S. The concepts of maximum permissible exposure. Radiology. Vol. 58 (1952). p. 639

St56 Sterner, J.H. Methods of establishing threshold limit values. Industrial Hygiene Quarterly. Vol. 17 (1956). p. 273-274

St62 Stokinger, H.E. Threshold limits and maximal acceptance concentrations. Archives of Environmental Health. Vol. 4 (1962). p. 115-117

St70 Stokinger, H.E. Criteria and procedures for assessing the toxic responses to industrial chemicals. In: Permissible levels of toxic substances in the working environment. Geneva : ILO, 1970. p. 36-52

St72 Stokinger, H.E. Concepts of thresholds in standards setting. Archives of Environmental Health. Vol. 25 (1972). p. 153-157

St73 Stokinger, H.E.; Scheel, L.D. Hypersusceptibility and genetic problems in occupational medicine - a consensus report. Journal of Occupational Medicine. Vol. 15 (1973). p. 564-573

St74 Stewart, R.D.; Peterson, J.E.; Newton, P.E. et al. Experimental human exposure to propylene glycol dinitrate. Toxicology and Applied Pharmacol. Vol. 30 (1974). p. 377-395

St86 Stokinger, H.E. Letter to the editor. American Industrial Hygiene Association Journal. Vol. 47 (1986). p. A-16

Swe82 Consensus report for diisocyanates. In: Scientific basis for Swedish occupational standards : 2. Solna, Sweden : National Board of Occupational Safety and Health, 1982. p. 60-68

Sy52 Symanski, H. (Severe health injuries resulting from occupational exposure to nitroglycerol). Arch Hyg Bakteriol. Vol. 136 (1952). p. 139-158

Syd84 Symanski, H. Why a discussion about "intoxications through nitroglycerol" again? Proceedings of the 1984 Medican conference, Calgary, Alberta, Canada

TLV85 Threshold limit values and biological exposure indices for 1985-86. Cincinnati, Ohio : ACGIH, 1985

Ta71 Taylor. L.S. Radiation protection standards. Ohio : CRC Press, 1971

Ta75 Takeuchi, Y.; Mabuchi, C.; Takagi, S. Polyneuropathy caused by petroleum benzene. International Archives of Occupational and Environmental Health. Vol. 34 (1975). p. 185-197

Ta80 Taylor, L.S. Organizations for radiation protection - the operations of the ICRP and NCRP 1928-1974 (DOE/TIC - 10124). Springfield, VA : NTIS, 1980. p. 4-21

Ta81 Taylor, L. Guest editorial - Technical accuracy in historical writing. Health Physics. Vol. 40 (1981). p. 595-599

Ta83 Takenaka, S.; Oldiges, H.; Konig, H.; Hochrainer, B.; Oberdorster, G. Carcinogenicity of cadmium chloride aerosols in Wistar rats. Journal of the National Cancer Insitute. Vol. 70 (1983). p. 367-371

Th74A Theriault, G.P.; Burgess, W.A.; DiBerardinis, L.J.; Peters, J.M. Dust exposure in the Vermont granite sheds. Arch. Environ. Health. Vol. 28 (1974). p. 12-17

Th74B Theriault, G.P.; Peters, J.M.; Fine, L.J. Pulmonary function in granite shed workers of Vermont. Archives of Environmental Health. Vol. 28 (1974). p. 18-22

Th74C Theriault G.P.; Peters, J.M.; Johson, W.M. Pulmonary function and roentgenographic changes in granite dust exposure. Archives of Environmental Health. Vol. 28 (1974). p. 23-27

Ti63 Tipton, I.H.; Cook, M.J. Trace elements in human tissue : II : adult subjects from the United States. Health Physics. Vol. 9 (1963). p. 103-119

Ti68 Tiller, J.R.; Schilling, R.S.F.; Morris, J.N. Occupational toxic factor and mortality from coronary heart disease. British Medical Journal. Vol. .4 (1968). p. 407-411

To79 Tolonen, M.; Nurminen, M.; Hernberg, S. Ten-year coronary mortality study of workers exposed to carbon disulfide. Scandinavian Journal of Work, Environment and Health. Vol. 5 (1979). p. 109-114

Tr66 Trainor, D.C.; Jones, R.C. Headaches in explosive magazine workers. Archives of Environmental Health. Vol. 12 (1966). p. 231-234

Ts66 Task group on lung dynamics. ICRP task group on lung dynamics. Health Physics. Vol. 12 (1966). p. 173

Ts67 Tsuchiya, K. Proteinuria of workers exposed to cadmium fume : the relationship to concentration in the working environment. Archives of Environmental Health. Vol. 14 (1967). p. 876-880

Tu24 Turner, J.A. Mercurial poisoning. Public Health Report. Vol. 39 (1924). p. 329-341

Tu56 Turrian, H.; Grandjean, E.; Turrian, V. Industrial hygiene and medical studies in mercury plants. Schweiz. Med. Wochenschr. Vol. 38 (1956). p. 1091-1096

US71 The U.S. Army Environmental Hygiene Agency : Special Study No. 99-005-72. Barraboo, WI, 1971

Up80 The UpJohn Company. Precautions for the proper usage of polyurethanes, polyisocyanurates and related materials. (Technical bulletin 107). 2nd edition. Zalamazoo, Michigan, 1980

Vi70 Viola, P.L. Carcinogenic effect of vinyl chloride. X International Cancer Congress, Houston, Abst., Vol. 29 (1970)

Vo37 Von Oettingen, W.F. The halogenated hydrocarbons : their toxicity and potential dangers. Journal of Industrial Hygiene and toxicology. Vol. 19 (1937). p. 349-448

Vo79 Von Reinl, W.; Weber, H.; Greiser, E. Epidemiological study on mortality on VC-exposed workers in the Federal Republic of Germany. Medichem. September, 2-8, 1979

WHO76 World Health Organization. Environmental health criteria 1 : mercury. Geneva : WHO, 1976

WHO79 Environmental health criteria 10 : carbon disulfide. Geneva : WHO, 1979

WHO80 World Health Organization : technical reports series 647. Geneva, 1980.

WHO84 World Health Organization. Fluorine and fluorides. Geneva : WHO, 1984

Wa76 Waldron, H.A. In: Lecture notes on occupational medicine. London : Blackwell Pub., 1976

Wa78 Waldbott, G.L.; Lee, J.R. Toxicity from repeated low-grade exposure to hydrogen fluoride - case report. Clinical Toxicology New York. Vol. 13 (1978). p. 391-402

War76 Ward, A.M.; Udnoon, S.; Watkins, J.; Walker, A.E.; Darke, C.S. Immunological mechanisms in the pathogenesis of vinyl chloride disease. Brit. Med. J. Vol. 1 (1976). p. 936-938

We74 Wegman, D.H.; Pagnotto, L.D.; Fine, L.J.; Peters, J.M. A dose response relationship in TDI workers. Occupational Medicine. Vol. 16 (1974). p. 258-260

We77 Wegman, D.H.; Peters, J.M.; Pagnotto, L.; Fine, L.J. Chronic pulmonary function loss from exposure to toluene diisocyanate. British Journal of Industrial Medicine. Vol. 34 (1977). p. 195-200

We81 Weill, H.; Butcher, B.; Dharmarajan, V.; Glindmeyer, H.; Jones, R. et al. Respiratory and immunologic evaluation of isocyanate exposure in a new manufacturing plant. Washington, D.C. : U.S. Department of Health and Human Services; National Institute for Occupational Safety and Health (NIOSH contract no. 210-75-306), 1981

We82 Wegman, D.H.; Mush, A.W.; Main, D.M.; Pagnotto, L.D. American Journal of Industrial Medicine. Vol. 3 (1982). p. 209

Wh80 White, D.A. Hydrofluoric acid - a chronic poisoning effect. Journal of the Society of Occupational Medicine. Vol. 30 (1980). p. 12-14

Wh84 White, J.W. Jr. Hydrofluoric acid burns. Cutis. Vol. 34 (1984). p. 241-244

Wi31 Wintz, H.; Rump, W. Protective measures against dangers resulting from the use of radium, roentgen, and ultra violet rays. Geneva : League of Nations, C.H., 1931

Wi64 Williamson, K.S. Studies of diisocyanate workers. Trans. Assoc. Ind. Med. Of. Vol. 14 (1964). p. 81-88

Wo82 Woolrich, P.F. Toxicology, industrial hygiene and medical control of TDI, MDI and PMPPI. American Industrial Hygiene Association Journal. Vol. 43, no. 2 (1982). P. 89-97

Ya67 Yamada, S. Intoxication polyneuritis in the workers exposed to n-hexane. Japanese Journal of Industrial Medicine. Vol. 9 (1967). p. 6551-659

Yo75 Yoshida, Y.; Watanabe, M.; Kono, K. Experimental studies on the percutaneous absorption of hydrofluoric acid and fluorine content of the organs. Japanese Journal of Industrial Health. Vol. 17 (1975). p. 281-287

23.0 GLOSSARY

A-1:
ACGIH classification of chemicals which are confirmed human carcinogens.

A-2:
ACGIH classification of chemicals which are suspected of having carcinogenic activity in humans.

Absorbed dose:
Energy imparted by ionizing radiation per unit mass.

$D = \frac{dE}{dm}$ Joules per kilogram

American Conference of Governmental Industrial Hygienists (ACGIH):
The organization which has developed the standards and philosophy for workplace chemical exposures in the Western world.

Annual Limit of Intake (ALI):
The activity of a radionuclide which taken alone would irradiate an average person to the limit set by the ICRP for each year of occupational exposure.

As Low as Reasonably Achievable (ALARA):
A concept of optimization of radiation protection. The acronym is not specifically used by the ICRP.

Biological Exposure Index (BEI):
A warning dose level of a chemical or one of its metabolites measured in exhaled air, body fluids or tissues. BEIs are intended to provide an indication of worker exposure to a chemical. Only six BEIs are presently used. The concept is new and controversial.

Ceiling Limit:
The concentration that should not be exceeded during any part of the working exposure.

Committed Dose Equivalent:
The time integral of the dose equivalent rate in a particular tissue that will be received by an individual following an intake of radioactive material into the body. Applies essentially to long-term effective half-lived radionuclides.

Derived Air Concentration (DAC):
That concentration of a radionuclide in air which if breathed by an average person for a working year of 2,000 hours under conditions of light activity would result in the ALI by inhalation.

Designated Substance:
A substance regulated under the Occupational Health and Safety Act of the Ontario Ministry of Labour.

Detriment:
The mathematical expectation of the amount of harm in an exposed group of people taking into account both the probability and the severity of the different possible harmful effects.

Dose Equivalent (H):
A measure of ionizing ray absorption normalized for effect in humans.
H= DQN, Q is quality factor; N is the product of all other modifying factors - currently taken as unity.

International Commission on Radiological Protection (ICRP):
The organization which has developed standards and concepts for ionizing radiation protection.

Maximum Allowable Concentration (MAC):
An exposure limit system based on the use of ceiling values. Now used largely by Soviet and Eastern European Countries.

Maximum Permissible Concentration (MPC):
Refers to radioactive substances measured in air.

National Institute for Occupational Health and Safety (U.S.A.) (NIOSH):
A federal U.S. organization which suggests chemical exposure levels based on health criteria alone.

Non-stochastic Effect:
Used in radiation protection. An effect in which the severity of the effect varies with the dose. A threshold dose is generally assumed to exist.

Occupational Health and Safety Administration (U.S.A.) (OSHA):
A federal U.S. agency for matters relating to regulation enforcement in the workplace.

Short-Term Exposure Limit (STEL):
The concentration to which workers can be exposed continuously for a short period of time without suffering from 1) irritation, 2) chronic or irreversible tissue damage, 3) narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency. A STEL is not a separate independent exposure limit and cannot be used to exceed the time-weighted average. A STEL is a 15-minute time-weighted average exposure which should not be exceeded at any time during the workday, even if the 8-hour time-weighted average is within the TLV. Exposures at the STEL should not be longer than 15 minutes and should not be repeated more than 4 times a day. There should be at least 60 minutes between successive exposures at the STEL.

Stochastic Effect:
An effect involving the probability of an injury due to ionizing radiation in an affected population. For any individual in that population it will or will not occur. The severity of the occurrence is not taken into account.

Threshold Limit Value (TLV):
A copyrighted term of the American Conference of governmental Industrial Hygienists (ACGIH) and used to describe their numerical exposure standards. There are three types of TLVs: time-weighted averages (TWA), short-term exposure limits (STEL) and ceiling values (TLV-C).

Time-weighted Average (TWA):
Is the airborne concentration of a chemical for a normal 8-hour workday, and 40-hour workweek to which nearly all workers may be repeatedly exposed, day-after-day, without adverse effect.

X-Rays:

Penetrating electromagnetic radiation produced by bombarding a metal target by high voltage accelerated electrons in an evacuated tube. The rays originate in the extranuclear part of the atom. Also called Roentgen rays.

TABLE 1

Origin of Exposure Limits for Workplace Chemicals in Canadian Jurisdictions

Canada (Federal):

ACGIH TLVs and BEIs for 1985-86 are referenced in section 10.21(1)(a) of the Canada Dangerous Substances Regulations (C.R.C. 1978, c. 977, as amended) made under the Canada Labour Code (R.S.C. 1970, c. L-1, as amended).

Alberta:

Occupational exposure limits (8 hour and 15 minute) listed in Schedule A, Table 1, are referenced in section 2.1 of the Chemical Hazards Regulation (Alta. Reg. 8/82) as amended by Alta. Reg. 242/83 made under the Occupational Health and Safety Act (R.S.A. 1980, c. 0-2). The occupational exposure limits of Alberta appear very similar to the TLVs of ACGIH. A few chemicals have different standards and reflect the specific requirements of the province for those chemicals.

British Columbia:

Permissible concentrations of airborne contaminant substances (8 hour and 15 minute limits) are referenced in section 13.01 and are listed in Appendix A of the Industrial Health and Safety Regulations (B.C. Reg. 585/77, as amended by B.C. Reg. 374/79; B.C. Reg. 71/82 126/82 (with erratum gazetted June 1, 1982) made under the Workers' Compensation Act (R.S.B.C. 1979, c. 437). The permissible concentration in British Columbia correspond to the 1976 TLVs of ACGIH. A few chemicals have different standards and reflect the specific requirements of the province for those chemicals.

Manitoba:

The current ACGIH TLVs are used by government safety and health officers, who can exercise a degree of discretion in determining acceptable exposure limits in given situations. TLVs are not referenced by the Workplace Safety and Health Act (S.M. 1976, c. 63, C.C.S.M., c. W210. as amended) or in the Regulation respecting the proper protection against injury of workers in work places, and respecting the protection of other persons from risks to their safety or health arising out of activities in work places (Man. Reg. 204/77, made under the above Act).

TABLE 1 cont'd

Origin of Exposure Limits for Workplace Chemicals in Canadian Jurisdictions

New Brunswick:

The ACGIH TLVs for 1976 are referenced in section 8(4) of the Occupational Safety Code Regulations (N.B. Reg. 77-1) made under the Occupational Health and Safety Act (S.N.B. 1983, c. 0-0.2), as amended).

Newfoundland:

The ACGIH TLVs 'currently established by "ACGIH"' (i.e. the most recent edition) are referred in clause 25(5)(a) of the Occupational Health and Safety Regulations, 1979 (Nfld. Reg. 104/79; as amended by Nfld. Reg. 7/80; Nfld. Reg. 921/80; Nfld. Reg. 329/80; Nfld, Reg. 143/82) made under the Occupational Health and Safety Act (R.S. Nfld. 1978, c. 23 as amended).

Nova Scotia:

The ACGIH TLVs for 1976 "and its subsequent amendments or revisions" are referenced in section 4 of the Occupational Health Regulations (N.S. Reg. 0.c 76-1510 December 21, 1976) made under the Public Health Act, now called the Health Act (R.S.N.S., 1967, c. 247).

Northwest Territories:

The "latest edition" of the ACGIH TLVs are referenced in section 31 of the General Safety Regulations (R.S.N.W.T. 1974, c. S-1, as amended) made under the Safety Act (R.S.N.W.T. 1974, c. S-1, as amended).

Ontario:

With a few exceptions including those noted below, TLVs in the most recent edition of the ACGIH TLV booklet are used by the inspectorate branches of the Occupational Health and Safety Division of the Ministry of Labour. The ACGIH TLVs for 1979 are referenced in section 279 of Regulations for Mines and Mining Plants (R.R.O. 1980, Reg. 694) for purposes of section 20 of the Occupational Health and Safety Act (R.S.O. 1980, c. 321).

TABLE 1 cont'd

Origin of Exposure Limits for Workplace Chemicals in Canadian Jurisdictions

Ontario (cont'd):

Exposure limits for some chemicals are found in the Designated Substance regulations made under subsection 41(2) 14 of the Occupational Health and Safety Act (R.S.O. 1980, c. 321, as amended). (Designated substances include acrylonitrile, arsenic, asbestos, asbestos on construction projects and in buildings and repair operations, benzene, coke oven emissions, isocyanates, lead, mercury, silica and vinyl chloride). As of 6th December 1986 all ACGIH TLVs will be legislated into Ontario law.

Prince Edward Island:

Current ACGIH TLVs are used as guidelines but not referenced by regulation. There is provision to set health and safety standards under section 34(a) of the Occupational Health and Safety Act (S.P.E.I. 1985, c. 36). However sections 1 to 4 and 6 to 35 of this Act are not yet proclaimed in force.

Quebec:

Average concentrations (8-hour) and maximum concentrations (for 15 minutes) are referenced in section 5 and are listed in Schedule A of the Quebec Regulation respecting the Quality of the Work Environment (O.C. 3845-80 as amended by O.C. 576-82) under the Environment Quality Act an Act Respecting Occupational Health and Safety (R.R.Q. 1981, s-2.1, r. 15); original French language version A.C. 3169-79, Règlement Rélatif à la Qualité du Milieu de Travail).

Saskatchewan:

Work place contamination limits are referenced in section 73 and are listed in Appendix VI of the Occupational Health and General Regulations (R.R.S., c. 0-1, Reg. 1) made under the Occupational Health and Safety Act (R.R.S. 1978, c. 0-1, as amended). The contamination limits of Saskatchewan appear very similar to the TLVs of ACGIH.

TABLE 1 cont'd

Origin of Exposure Limits for Workplace Chemicals in Canadian Jurisdictions

Yukon Territory:

ACGIH TLVs are applied as a matter of policy; however, inspectors can exercise a degree of discretion in determining acceptable exposure limits in given situations. No list of exposure limits is referenced in any regulations, however, section 26 of the Accident Prevention Regulations (C.O. 1963/1) allows an inspector to require that ventilation be provided to reduce the contamination to at least the "recognized maximum allowable concentration for the impurity involved". These regulations were made under the Public Health Ordinance (O.Y.T. 1983, (3rd), c.6).

"Permissible Concentrations" are listed in the proposed Occupational Health and Safety Regulations made under section 54(2)(h) of Occupational Health and Safety Act (S.Y.T. 1984, c.46/0.05) (not yet proclaimed)

TABLE 2

The Ten Chemicals Chosen for this Study

Substance	Chronic Disease
Toluene 2,4-Diisocyanate	Respiratory sensitization, lung function decrease.
Hydrofluoric Acid	Fluorosis. A degenerative bone condition of ten associated with gastrointestinal and other functional disorders.
n-Hexane	Peripheral neuropathy. A degeneration of the nerves in the extremities.
Carbon Disulfide	Coronary arteriosclerotic heart disease.
Cadmium	Kidney function impairment.
Mercury	Erethisim, psychosis and behavioural disturbances.
Cobolt	Hard metal disease of the lung (interstitial pneumoconiosis).
Nitroglycerine	Heart failure.
Silica	Silicosis. Interstitial fibrosis of the lung.
Vinyl chloride	Angiosarcoma. A unique tumour of the liver.

TABLE 3

Mercury Exposed Workers Grouped by Time-Weighted Average Exposure Levels*

Exposure Levels (mg/m^3)	Number of Workers	Percentage of Exposed Workers	Group No.
0.01	58	10.2	1**
0.01 - 0.05	276	48.7	2
0.06 - 0.10	145	25.6	3
0.11 - 0.14	61	10.7	4
0.15 - 0.23	-	-	-
0.24 - 0.27	27	4.8	5

* Adapted from Smith et al(Sm70)

** Control group

TABLE 4*

Excess Risk Factors for Inhalation of Vinyl Chloride:
Results Using a Single Exposure Group

Experimental Animal	Exposure Time (week)	Observation Time (week)(1)	Type of Tumour	No Effect Level (ppm)	Observed Excess Risk per ppm	Upper Confidence Limit on Excess Risk per ppm 99%
Sprague-Dawley Rat	52	135	Nephroblastoma	50	3.4×10^{-4}	2.1×10^{-3}
			Liver Angiosarcoma	50	3.4×10^{-4}	2.1×10^{-3}
			All Tumours	50	1.3×10^{-3}	4.3×10^{-3}
Sprague-Dawley Rat	17	86	Brain Neuroblastoma	500	0	1.5×10^{-4}
			All Tumours	500	4.6×10^{-5}	1.6×10^{-4}
Swiss Mice	30	61	Pulmonary Tumours	50	-2.2×10^{-4}	8.2×10^{-4}
			Mammary Carcinoma	50**	3.5×10^{-3}	6.4×10^{-3}
			Liver Angiosarcoma	50	3.5×10^{-4}	2.2×10^{-3}
			Angiosarcomas	50**	3.9×10^{-3}	6.9×10^{-3}
			Other than Liver or Other than Liver or Other vascular tumours			
			Epithelial Tumours of Skin	250	0	3.0×10^{-4}
			All Tumours	50**	4.9×10^{-3}	7.8×10^{-3}
Golden Hamsters	30	48	All Tumours	50**	2.6×10^{-3}	5.5×10^{-3}

NOTES: 1. Observation times for both exposed and unexposed animals were the same.
2. Results are reported only where there is a statistically significant difference between exposed and unexposed animals. Results concerning Zymbal Gland carcinoma are excluded.

* Adapted from Ministry of Labour report on the designation of vinyl chloride in Ontario(MOL85)

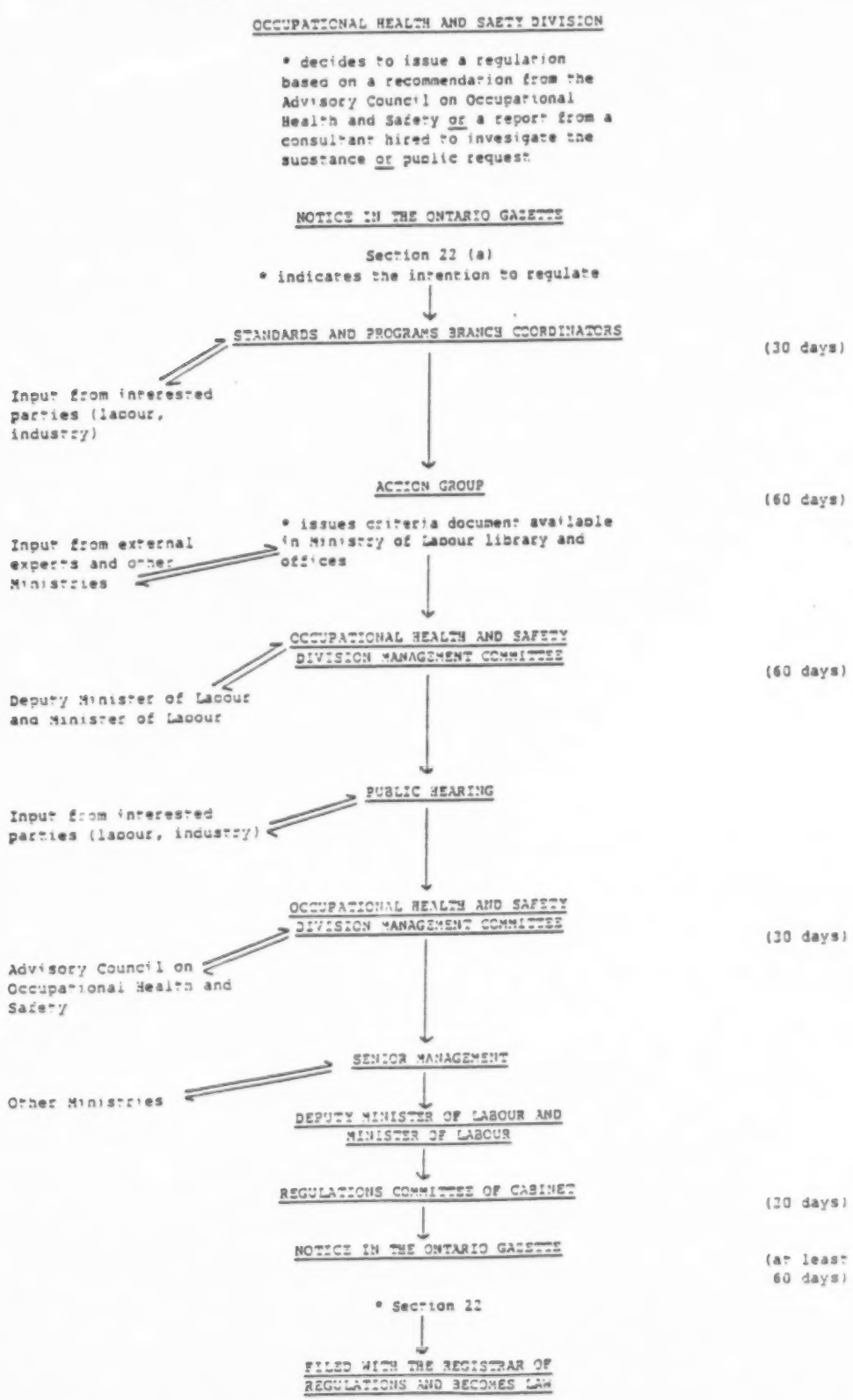
** Indicates that there is a significant difference in tumour frequency between control group and lowest exposure group.

TABLE 5

Summary of Factors Used by ACGIH in Standard Setting for Ten Chemicals

Chemical	Apparent Factors Considered in Recommended Standard by ACGIH or Ontario Ministry of Labour	Safety Factor
1. TDI	Human health data.	None
2. Hydrofluoric Acid	Animal data, human health data.	None
3. n-Hexane	Human health data.	x 4
4. Carbon Disulfide	Human health data, economics.	None
5. Cadmium	Human health data.	x 1.5
6. Mercury	Human health data, differences in organ dose between mercury vapour and mercury salts.	x 5 for vapour
7. Cobalt	Animal data, economic, technical implication for industry	Unknown
8. NG/EGDN	Human health data, economics for industry of maintaining sub-pharmaceutical levels	None
9. Silica	Human health data principle of low exposure correlates with low disease incidence. Technical feasibility.	None
10. Vinyl chloride	Lowest level technically achievable by industry (ACGIH), risk assessement extrapolation from animal data (MOL).	Unknown

Figure 1 - Details of the process followed by the Ontario Ministry of Labour in the development of designated substance standards.


OCCUPATIONAL HEALTH AND SAETY DIVISION
• decides to issue a regulation based on a recommendation from the Advisory Council on Occupational Health and Safety or a report from a consultant hired to invesigate the substance or public request
NOTICE IN THE ONTARIO GAZETTE
Section 22 (a)
• indicates the intention to regulate
STANDARDS AND PROGRAMS BRANCH COORDINATORS
(30 days)
Input from interested parties (labour, industry)
ACTION GROUP
(60 days)
• issues criteria document available in Ministry of Labour library and offices
Input from external experts and other Ministries
OCCUPATIONAL HEALTH AND SAFETY DIVISION MANAGEMENT COMMITTEE
(60 days)
Deputy Minister of Labour and Minister of Labour
PUBLIC HEARING
Input from interested parties (labour, industry)
OCCUPATIONAL HEALTH AND SAFETY DIVISION MANAGEMENT COMMITTEE
(30 days)
Advisory Council on Occupational Health and Safety
SENIOR MANAGEMENT
Other Ministries
DEPUTY MINISTER OF LABOUR AND MINISTER OF LABOUR
REGULATIONS COMMITTEE OF CABINET
(30 days)
NOTICE IN THE ONTARIO GAZETTE
(at least 60 days)
• Section 22
FILED WITH THE REGISTRAR OF REGULATIONS AND BECOMES LAW

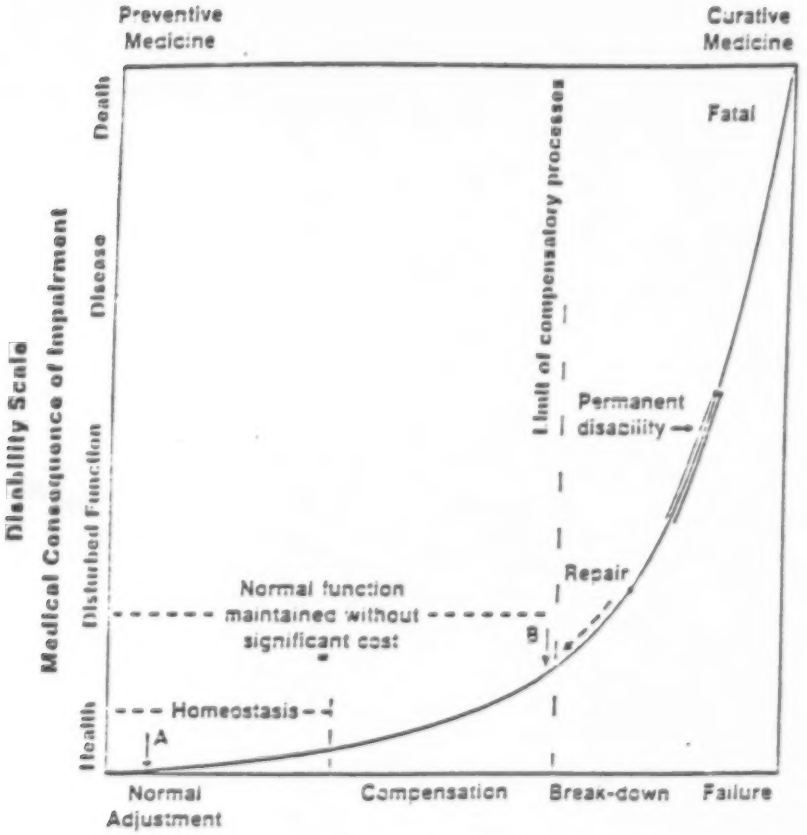



Figure 2 - The Impairment-Disability Curve (Ha62)